

SCIENCE

AUGUST 25, 1950



ADAPTING TO CALORIC RESTRICTION

HENRY L. TAYLOR AND ANCEL KEYS

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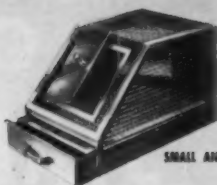
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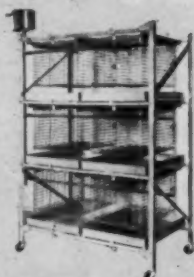
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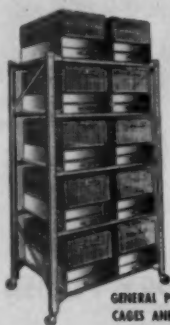
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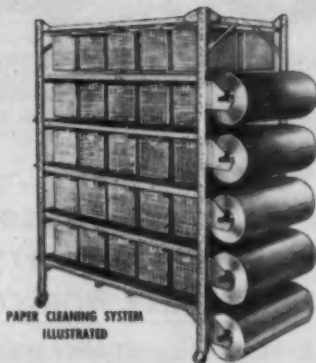
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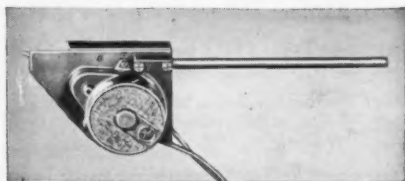
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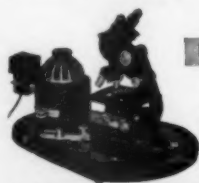
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Adaptation to Caloric Restriction

Henry Longstreet Taylor and Ancel Keys

The Laboratory of Physiological Hygiene, University of Minnesota, Minneapolis

EVER SINCE Claude Bernard pointed out the role of the internal environment in mitigating the impact of external stresses on the cellular machinery of the body, the question as to how the body makes adjustments to difficult or new conditions has been under scrutiny. The adaptations to such diverse stresses as anemia, pregnancy, low calcium intake, and exposure to high altitude and to heat have been described in some detail. To some stresses, such as cold, the human body makes favorable adjustments, but as yet the data are inadequate to define and explain the mechanisms involved. The problem of adaptation to caloric restriction has occupied a somewhat intermediate position. On the one hand, it has been recognized that extensive adaptations occur in inhabitants of famine areas (15), but no data of value from the field are available. On the other hand, a mild degree of caloric restriction has been studied in the laboratory, and some of the mechanisms that help to produce the observed adaptation have been described (2). However, the data necessary for a more complete quantitative description of the extent of adaptation under famine conditions have been made available only recently by the results of the Minnesota Experiment on semistarvation (8). The general conditions of this experiment have been described, and some of the results have been reported (4, 6, 12, 17, 19, 20).

The subjects were 32 conscientious objectors who were resident in the Laboratory of Physiological Hygiene for a year. Following three months of control studies, they underwent six months of semistarvation and then were studied during three months of rehabilitation. During the control period the subjects ate a diet that was adequate in protein, vitamins, and minerals, but that did not provide excessive amounts of any specific nutrient. The body weight of the group was maintained on 3,492 calories per day. The activity regimen that the men followed included a set schedule of routine laboratory and housekeeping chores, 20 miles of walking each week, and participation in a special educational program.

The semistarvation diet was instituted at the end of the control period and continued for six months. It provided an average of 1,570 calories daily, or slightly less than half the control intake, and consisted of potatoes, cabbage, turnips, and cereals, with only a few grams of animal protein a week. In other words, the men ate the kind of foodstuffs used in famine in northern Europe. Analysis of the diet showed that it contained an average of 54.5 grams of protein and 27.1 grams of fat a day. The mineral and vitamin intakes of the subjects during the semistarvation period were in the general range of the National Research Council Recommended Daily Allowances (21), with the exception of the intakes of riboflavin and vitamin A, which were roughly one-half the recommended standards.

At the end of six months on this diet the subjects had lost 24 percent of their body weight and showed the classical signs and symptoms of famine victims, namely, edema, anemia, polyuria, bradycardia, weakness, and depression.

The weight loss curve during the semistarvation period followed the law of diminishing decrements (3). At the end of the period the body weight was substantially constant. During the last three weeks the average loss of weight was only 0.13 kg per week. The dimensions of the adaptation to the imposed restriction of caloric intake are defined by the fact that, in the face of a 55 percent reduction, the subjects were able, for all practical purposes, to maintain caloric balance, but at a body weight reduced to 75 percent of the original prestarvation weight.

ADJUSTMENT TO STARVATION

The way in which this adjustment was achieved is revealed by a detailed analysis of the energy expenditure. The essential data are presented in Table 1. The mean basal metabolism was calculated from serial determinations made on every member of the subject group. The specific dynamic action (S.D.A.) was taken as 10 percent of the total caloric intake. The cost of activity was calculated as that part of the total intake not accounted for by basal metabolism plus the

TABLE 1
ESTIMATED PARTITION OF MEAN ENERGY EXPENDITURE IN
KILO CALORIES PER DAY OF 32 YOUNG MEN BEFORE
AND AFTER SIX MONTHS OF SEMISTARVATION

	Before	After	Δ	Δ , as % of total Δ	Δ , as % of control
Basal metabolism	1,576	962	614	31.9	39
Specific dynamic action	349	137	192	10.0	55
Cost of activity	1,567	451	1,116	58.1	71
Total	3,492	1,570	1,922		

S.D.A. This procedure is justifiable at the balance point. The data demonstrate that a little less than two-thirds of the total saving in calories may be assigned to the cost of physical activity. We may ask, How much of this reduction was due to a decrease in activity and how much to a smaller cost of work? The subjects suffered a marked loss of strength and endurance as the starvation period progressed (11). The men commented that they felt as if they were rapidly growing old. They felt weak and they tired easily. They moved cautiously, climbing stairs one step at a time, and obviously reduced unnecessary movements to a minimum. All observations indicated that voluntary physical activity was markedly curtailed at the end of the starvation period.

The cost of specified work was investigated in 10 of these men, who walked on a motor-driven treadmill at 3.5 miles per hour and a 10 percent grade before, in the middle, and at the end of the semistarvation period. It was found that the oxygen consumption during work was linearly related to the body weight, regardless of whether the values were taken in the control period, or after twelve or twenty-four weeks of semistarvation (11). Respiratory quotient measurements in work showed no substantial change at any time; in other words, the calorie value per unit of oxygen consumption was constant. The average cost of this standard work, per kg of body weight per minute, was 0.111, 0.110, 0.111 calories for the control, and for the twelfth and twenty-fourth weeks of semistarvation, respectively. The energy cost of a given task was reduced at the end of starvation in direct proportion to the loss of body weight. Accordingly, as there was no change in efficiency, the percentage reduction in activity during the six months of starvation should be corrected for the change in body weight (minus 24 percent). In these terms, the activity level of the control period would cost 1,200 calories for the body weight at the end of semistarvation. But the actual cost of activity at that time was reduced to 499 calories. In terms of the observed total reduction in the cost of physical activity, 60 percent is due to decrease

in the tasks undertaken and 40 percent to a decrease in the cost of performing these tasks.

This analysis of the way in which the cost of activity was reduced assumes that physical activity consisted in moving the body from place to place. Such an assumption is justified as a first approximation when dealing with men who are engaged in occupations like those of our subjects; it is not applicable to persons engaged in heavy physical work, where moving external objects constitutes a large part of the total work.

In a somewhat similar manner we may examine the observed reduction in basal metabolism. How much of this decrease is due to a loss of metabolizing tissue, and how much to a change in the rate of metabolism of the remaining tissue?

In the Minnesota Experiment, an effort was made to estimate the mass of the actively metabolizing tissue (9). To obtain this figure, measurements were made of the total body fat (specific gravity method), extracellular fluid (thiocyanate space), and blood volume (blue dye). These measurements define a large fraction of the metabolically inert portion of the body but do not include the skeleton. The x-ray density of the bones was determined from roentgen films, and it was shown that no important change took place as the result of starvation.¹ It was assumed that 4 percent of the original (prestarvation) body weight was contributed by the minerals of the bones. The metabolizing, or "active," tissue was then calculated as the body weight less the weight of the bone mineral, extracellular fluid volume (including plasma), and fat. Inasmuch as the extracellular fluid volume and fat determinations measure these items in the bones, it is felt that this calculation gives a reasonable approximation of the mass of the "active tissue." It should be noted, however, that the calculation reveals nothing about the intracellular water. In the starving rat, at least, the concentration of intracellular water in muscle and other active tissues remains constant when the serum protein concentration has not dropped below 5.5 grams per 100 ml (14).

The average mass of "active tissue" for the 32 men in the Minnesota Experiment was estimated, in this way, to be 39.95 kg in the control period and 29.19 kg after six months of semistarvation. The loss of 27.4 percent of "active tissue" indicates that the body weight measurement, which showed a 24 percent loss, was lower than the loss of "active tissue" by a small amount.

The metabolic rate during the six months of semistarvation decreased 31.2 percent, when the data are calculated as ml of oxygen consumption per square

¹ We are indebted to Pauline Beery Mack for these measurements.

meter of body surface (10). When the oxygen intake is calculated as ml per kg of body weight, the change during semistarvation amounts to 19.3 percent. Finally, when the metabolic rate is expressed as ml per kg of "active tissue," the decrease is only 15.5 percent. It appears that the conventional method of expressing basal metabolic rates in units of body surface does not properly indicate the intensity of metabolism of the cells of the body during starvation. The oxygen intake per kg of "active tissue" may be taken to give the nearest approximation to the actual metabolic rate of the cells of the body. The data indicate that the greater part of the decrease in the B.M.R. (65 percent) in starvation reflects the shrinkage of the metabolizing mass of tissue, and the smaller part (35 percent) should be ascribed to a decrease in the intensity of metabolism. From metabolic studies on severely undernourished persons in western Europe (1), it has been suggested that the intensity of metabolism in the "active" cells may even be undiminished in semistarvation, but the computations assume that the Minnesota findings on extracellular water and fat applied quantitatively to their subjects. In any case, these studies on "natural" famine victims are at least in rough agreement with the present conclusion that semistarvation does not produce any great change in the metabolic rate per unit mass of living cells.

We do not suggest that the rate of basal O_2 consumption of all tissues in the body was reduced by 15 percent. Kleiber (13) has shown that, in the rat, during starvation the decrease of the metabolic rate of various isolated organs and tissues is not constant; the present computation refers only to the sum total of basal metabolism. Finally, in considering the cause of the decrease in the metabolic rate per unit of "active tissue," it should be remembered that a small decrease in body temperature has a definite effect on the metabolic rate. In the Minnesota Experiment the body temperature decreased $0.74^\circ C$ after twelve weeks of semistarvation. If we assume a temperature coefficient (Q_{10}) of 2.0, 10 percent of the 32 percent decrease in basal metabolism that had occurred at this time could be accounted for by the decline in body temperature. It is interesting to note that at the end of twenty-four weeks of semistarvation the average body temperature differed from that of the control period by only $0.126^\circ C$. This may indicate that the temperature-regulating mechanism had somehow become adjusted so as to maintain a more normal body temperature in the face of continued food restriction. It should be remarked, however, that the semistarvation began in February, so the end of this phase of the study occurred in the summer. In any case, after six months of semistarvation in the Minnesota Experiment, no appreciable part of the reduced energy ex-

penditure could be explained on the basis of a reduced tissue temperature.

The concentration of the serum proteins is an important factor in the maintenance of a normal distribution of fluid between the plasma and the extracellular fluid. The Minnesota subjects showed a selective use of body protein during starvation that maintained the total circulating serum proteins at a substantially normal level, whereas protein was lost by the tissues and cells in large amounts (19). Although the concentration of the serum protein decreased slightly, this could be accounted for by a parallel increase in serum volume. The distribution of fluids between serum and extracellular fluid was well maintained in our subjects. This was shown by the fact that the absolute extracellular volume increased by only 4.3 percent, and serum volume increased by only 8 percent, as the result of six months of semistarvation (4). With continued starvation, of course, a point is eventually reached where the plasma proteins can no longer be safeguarded and there is development of severe hypoproteinemia, with all the attendant difficulties.

The changes in energy expenditure during semistarvation are of great importance in helping the organism to survive on a low level of food intake. But there are many other adjustments in the body of the starving man which mitigate the consequences of the negative caloric balance. A few of these may be noted.

OTHER PROTECTIVE CHANGES

In spite of the adaptation in the energy expenditure, the starving body is forced to use some of its own protein for fuel. The circulating plasma proteins would seem to be most readily available for this purpose, but their preferential destruction would quickly have disastrous consequences.

Another example of a differential metabolic destruction of special tissues that is of obvious utility to the organism in survival is provided by the brain. This tissue loses a smaller fraction of its initial weight during a period of severe starvation (5). The brain, skeleton, and serum proteins remain almost intact, whereas fat, muscle, liver, and skin undergo large losses.

In spite of statements to the contrary by every major textbook of physiology since 1900, the heart undergoes considerable loss of muscle mass during acute and chronic starvation. Jackson (5) has reviewed the results of experiments on animals and autopsy material, which all indicate that the percentage loss of heart weight is 70-90 percent of the percentage loss of the body weight. In the Minnesota Experiment roentgenkymographic estimations of heart

size indicated that the heart volume decreased by 17 percent (12). In other words, the relative reduction in the heart was not materially less than that of the body as a whole. Recent necropsy data are in agreement. But analysis of the cardiac function reveals adaptations which safeguard the heart in starvation. Measurements of pulse rate, blood pressure, stroke volume, and the time of mechanical systole before and after semistarvation made it possible to calculate the work of the heart (12). The work done by the heart decreases by about 50 percent as the result of starvation, or 20 percent more than would correspond to the decrease in oxygen intake. This represents a protective change that may be designated an adaptation without inquiring as to cause and effect.

Man, therefore, can achieve a not inconsiderable adaptation to the caloric restriction. The manner in which the adaptation is achieved, however, is, in part, quite different from the way in which the body adapts to such stresses as high-altitude exposure, heart disease, or an increase in the environmental temperature. It is clear that much of the adaptation is an automatic consequence of the use of the body itself as fuel for the metabolism. The life of the organism is prolonged or maintained closer to normal than would otherwise be the case by the rather desperate expedient of reducing the mass activity of the organism. This mechanism, it seems to us, is entirely passive and produces major limitations and stresses of its own. In contrast, the man who is faced with the problem of existence in an atmosphere which has a low partial pressure of oxygen and a reduced number of oxygen molecules per unit volume achieves a more positive adaptation. He reduces his demand for high rates of oxygen supply by reducing the intensity of physical work, but does not alter his oxygen use or rate of life at rest or with moderate activity. Adaptive mechanisms provide oxygen to the body in normal amounts for all except extreme exertion. The changes

include an increase in red cell concentration, a higher rate of pulmonary ventilation, and a change in the acid-base balance of the blood (7).

The man who travels from a cool to a hot environment adapts to this stress by a more efficient elimination of heat through an improved cardiovascular performance (16, 18) and, apparently, through a small reduction in basal heat production. Safety in a high rate of sweating is assured by an adaptation in the composition of the sweat. Mechanisms of this kind may be classed as active or positive adaptations, and they do not in themselves impose major limitations on performance. In the semistarved individual the reduction of oxygen consumption per unit of active tissue and the lowered cardiac work load at rest appear to be examples of active adaptation to stress of caloric restriction.

The Minnesota Experiment has provided a quantitative description of a few facts concerning the adaptation of man to caloric restriction. Adaptation in general may be defined as the adjustment of the organism to its life situation. If a new or changed life situation induces changes in the organism that enable it to meet the new life situation more effectively than would otherwise be the case, then the changes are adaptive. When these changes result in full preservation of the normal "freedom" of the organism, in Claude Bernard's sense, then perfect adaptation has been achieved. The adaptations that occur in stressful, i.e., biologically difficult, situations are generally compromises. The maximal or best adaptation maintains the freedom of the organism and its prospects of survival at the highest level compatible with the situation. It is clear that the changes due to semistarvation permit man to meet the altered situation produced by caloric restriction with moderate success. The fact that these adaptive mechanisms do not result in a complete and unequivocally favorable adjustment does not detract from the advantages gained.

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Meetings of the A.A.A.S. and A.I.B.S.: A Joint Statement

Clarence J. Hylander,¹ Howard A. Meyerhoff,² and Raymond L. Taylor³

THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE at this time is engaged in planning future meetings for its affiliated scientific societies, and is completing arrangements for the 1950 meeting at Cleveland, December 26-30. At the same time, the American Institute of Biological Sciences is engaged in completing arrangements for the 1950 meeting of biological societies at The Ohio State University, September 11-13, and is exploring the available campus facilities for possible future meetings of biological societies. To some biologists, these activities have appeared competitive, and so many queries have come to the attention of the secretaries of the two organizations that a joint statement seems the best means of providing some of the answers and of clarifying objectives.

The American Institute of Biological Sciences has a variety of functions, as stated in its Constitution; one of these is rendering assistance to biological societies in matters of common concern, such as arrangement of joint annual meetings, should any member society request it. Like the 216 scientific societies affiliated or associated with the AAAS, the 16 biological societies of the AIBS have varying degrees of affinity with respect to meetings. Some have customarily met with the AAAS; others have regularly arranged independent meetings; a few have chosen meeting associates and locales to accomplish immediate objectives. Like the AAAS, the AIBS has neither the power nor the desire to force any change in pattern or tradition upon its affiliates.

Scientific societies that are members of both AIBS and AAAS should realize that the objectives of the two organizations are different. The American Association for the Advancement of Science, as its name implies, was founded to serve the interests of *all* science and *all* scientists. At its annual meetings the AAAS endeavors, not so much to put on a specialized program for each individual discipline, as it does to explore the interdisciplinary relationships between and among the several fields of pure and applied science. The 17 sections and subsections of the Association may, it is true, plan specialized programs, and those societies that meet with the Association are expected to stress their own fields of specialization. But all of them have the opportunity to meet jointly with other groups and to enjoy the fruits of cross-fertilization that have opened up so many horizons in scientific

theory, in laboratory and field research, and in application. The American Institute of Biological Sciences, on the other hand, was founded to serve the interests of biologists, and the application of biological research to human welfare. At any joint annual meeting of biological societies under its sponsorship, the AIBS serves chiefly as a central organizing agency for making all arrangements necessary to insure a satisfactory meeting and to relieve the individual societies of as much detailed responsibility as possible.

In offering its services to affiliates, the AAAS gives each one complete autonomy in arranging its own program. By making use of the downtown hotels in large cities the AAAS can, and does, insulate each affiliate from the simultaneous activities of other scientific groups to the degree it may desire, and in this way it achieves the same effect as could be attained in a small, independent meeting. Members have the option of seeing exhibits that may not strictly relate to their own field, of hearing general lectures, or of playing "hooky" to learn what goes on in other societies—or even what comes off in the local burlesque theater!

Meetings arranged by the AIBS, on the other hand, are deliberately planned for an academic atmosphere, with the number of participants therefore naturally limited to the facilities of the university selected. Such meetings are arranged to provide the physical setting and facilities appropriate to the type of meeting desired by the participating AIBS societies. Among the desires that have been expressed, and to which particular attention is being paid, are (1) smaller meetings than those involving many scientific societies, but larger than those than can be organized by an individual society; (2) greater coherence of subject matter than is possible or desirable in a general scientific convention, but broader in scope than can be achieved by a single organization; (3) use of campus facilities, or other similar locales; (4) avoidance of a Christmas meeting, with preference, at present, for a September meeting just before or after Labor Day.

The extent to which these desires can be met is severely limited. There are 16 constituent societies in the AIBS, with a nonduplicating membership of 14,000—a figure that is impressively large. It is evident that any meeting involving all, or most of, the member societies of the AIBS—and nonmember biological societies that, additionally, may wish to meet with it—could not be small. Furthermore, there are few campuses that can comfortably accommodate more

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than 2,500 visitors, even when universities are not in session. Thus, 2,500 becomes an upper limit of size if the Institute wishes to maintain some geographic mobility and, at the same time, avoid using the hotels of a few metropolitan centers.

The best time for meetings can be a subject of endless debate. Although the AAAS has not always scheduled its meetings during Christmas week (September, 1944, at Cleveland; March, 1946, at St. Louis; September, 1948, at Washington), it generally plans to utilize this period of the year because the universities are not in session and, despite family ties and customs, more scientists are freer then than at any other time of year. Hotel commitments are normally lighter during the holidays, facilities can be stretched to their utmost in any city selected, and maximum service can be obtained. It is a time when the commercial demand for auditorium space is low or non-existent, and when favorable arrangements can be made for the use of every type of facility that is necessary or desirable for a large meeting.

There are only a few periods in each year when university campuses are available. The best times are in June, following commencement but before service personnel has dispersed, summer maintenance work has begun, or summer sessions have been started; or in September, just before the fall semester begins. If dormitory accommodations and university restaurant facilities can be used, the cost of attending meetings can be reduced so far as these items are concerned. Here, again, sentiment is divided between those who wish to economize and those who wish, temporarily, to break away from an academic atmosphere and to explore metropolitan attractions.

It is clearly impossible to please everyone either in the timing, or in the locale, or in the type of meetings. It is partly for this reason that the AIBS and the AAAS, deliberately, are diverging in their choice of the time, place, and kind of meetings each of them will arrange. (That both organizations selected Ohio cities for their 1950 meetings was a coincidence.) In 1951, the AIBS-sponsored meeting will be at the University of Minnesota, the AAAS in Philadelphia; in 1952, the AIBS is considering a campus in the South-eastern states, and the AAAS will meet in St. Louis.

Because of the need to limit attendance to the restricted capacities of the cities or campuses selected, both AAAS and AIBS must know, well in advance, the wishes of their respective societies. Neither can accommodate all, or even a majority, without drastic alterations in its plans. There are, for example, but three localities in the country that can handle as large a convention as the 116th meeting of the Association at New York last December, yet there are obvious advantages in scheduling meetings in many other com-

munities. If it continues to preserve its traditional mobility, even the Association may be compelled to limit participation on the part of societies that make their wishes known too late, when meetings are scheduled in smaller cities. Thus, for both organizations, the need to plan ahead more than a year at a time is imperative; the need to know what meeting plans affiliated societies are making is no less urgent. Even now, as the Association is investigating available facilities for 1953, 1954, and 1955, it encounters prior reservations on hotel space in some cities.

If it were possible to do more than guess at the prospective attendance, the problems of the AIBS and the AAAS would be greatly simplified. But "guesstimates" are all that are available until the societies reach their decisions. Both the AAAS and the AIBS hope that they can continue to provide suitable physical facilities and to print general programs without special assessments or levies on participating societies. It must not be thought, however, that scientific meetings can be run without cost. AAAS meetings usually have been operated at substantial deficits, notwithstanding the offsetting income from registration fees and the sale of exhibition space. The AIBS faces the same situation. For this reason, both the AAAS and the AIBS expect that all scientists who attend their respective meetings will register and thus contribute their share to carrying the financial burden. The registration fees are kept at a minimum, but, with mounting costs everywhere, it cannot be expected that they will ever be less than \$2.00 to \$3.00.

Unless scientists meet to exchange views and laboratory experiences, their sciences are dead or dying. Few of them have the time to devote to the minutiae of arranging meetings, and it is inevitable that they—and their societies—should entrust this onerous task to organizations that have the staffs and the experience for this purpose. Meetings of any size are arranged, not by magic and miracle, but by hard and patient work for a year or more in advance. The final effectiveness of this work depends very largely on the cooperation received from the participating societies, and the support given by individual society members. The AAAS and the AIBS are confident that society officers and members will appreciate this mutuality of interests and responsibilities, not only at Columbus and Cleveland, in 1950, but at the meetings planned for subsequent years.

It will be most helpful to the AAAS and the AIBS if, at these meetings, the biological societies can decide on their meeting places for the next few years and will advise both the Association and the Institute of their decisions at their earliest convenience. Officers of the two organizations will be available for consultation at both Columbus and Cleveland.

Technical Papers

Nucleodepolymerase Activity of Precancerous Rat Liver¹

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Evidence has been obtained in this laboratory (1) of the occurrence of an irreversible liver cirrhosis, indicative of a preneoplastic state, in rats fed cooked polished rice and *p*-dimethylaminoazobenzene during 120 days. It is not clear how the azo dye operates to produce an altered equilibrium at the precancerous level in the economy of the liver cell.

The part played by nucleic acids in tumor production has been demonstrated by Caspersen and Santesson (2). Whether the altered desoxyribonucleic acid equilibrium in precancerous liver cells is the first step toward cellular malignancy or is only an accompanying phenomenon is not evident. Nevertheless, desoxyribonucleic acid synthesis appears intimately bound to the mitotic mechanism and to cellular division, so that any quantitative change in the desoxyribonucleic acid synthesis may well be the cause of abnormal cellular proliferation. Because studies of the chemical and enzymatic pattern of the nucleic acid in cancer tissue have revealed the net results of altered metabolism of nucleic acid, it was felt that similar studies during the transition period of carcinogenesis would help to elucidate the evolution nucleic acid metabolism may be undergoing during carcinogenesis.

TABLE 1
NUCLEODEPOLYMERASE ACTIVITY OF PRECANCEROUS RAT LIVER

Time, days	0	30	60	90	120	150
Ribonucleodepolymerase*	.09	.11	.13	.23	.18	.13
Desoxyribonucleodepolymerase†	9.4	10.7	13.9	16.5	13.5	11.1

* In terms of increase of mg acid soluble P after 2 hr incubation at 37° C. of a mixture of 1 ml of a 3% Na ribonucleate, 1 ml of tissue extract containing 0.40 mg N acid 1 ml of veronal acetate buffer at pH 7.

† In terms of decrease of viscosity, after ½ hr of incubation at 30° C. of a mixture of 3 ml of 1% Na desoxyribonucleate and 3 ml of tissue extract containing 1.23 mg N/ml.

Investigation of nucleodepolymerase activity was carried out according to the method described by Greenstein (3), who reported no change in depolymerase activity in normal liver and in transplanted hepatoma. We find no reference in the literature to the nucleodepolymerase activity of precancerous tissue and particularly of precancerous cirrhotic liver in rats fed *p*-dimethylaminoazobenzene. In view of the importance of these enzymes in the altered metabolism of nucleic acid, we have investigated the depolymerase activity of preneoplastic tissue.

¹ This investigation is part of a research project (No. 56) that is supported by a grant-in-aid from the National Cancer Institute of Canada, for which the authors are most grateful.

Albino white rats (Carworth Farms) were fed a diet of cooked polished rice with *p*-dimethylaminoazobenzene (0.06% concentration) supplemented with 1 g of fresh carrots per day. The nucleodepolymerase activity of rat liver was determined according to method described by

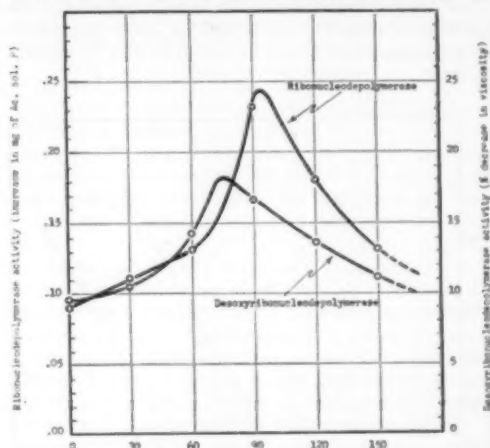


FIG. 1. Nucleodepolymerase activity of precancerous rat liver (time, days).

Greenstein, at 30-day intervals, for a period of 150 days on the basic diet. The ribonucleodepolymerase activity in normal rat liver was 0.09, which is a value similar to Greenstein's. The desoxyribonucleate, on the other hand, was found to be slightly higher (9.4), compared to 7.0 reported by Greenstein (4).

Our results to date on this precancerous cirrhotic liver indicate that the nucleodepolymerase activity varies appreciably in comparison with that of normal rat liver. The enzymatic activities of both depolymerases show a progressive increase up to maximum activity at 90 days, followed by progressive decrease to 150 days (Table 1).

The period of increased activity of the depolymerases (90-120 days) corresponds to the precancerous cirrhotic liver stage. It would appear that, once this transition stage of carcinogenesis has been reached, the depolymerase activity decreases and finally drops with the occurrence of the hepatoma to a normal level (Fig. 1). These findings indicate that the enzymes of nucleic acid metabolism behave differently during the transition stage of carcinogenesis than in the true neoplastic stage.

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Determination of DDT by Bioassay

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The widespread use of the insecticide DDT has brought about the problem of its residue in milk and other foods (1, 3). As a result, a simple rapid procedure for quantitative measurement of small amounts of DDT is urgently needed.

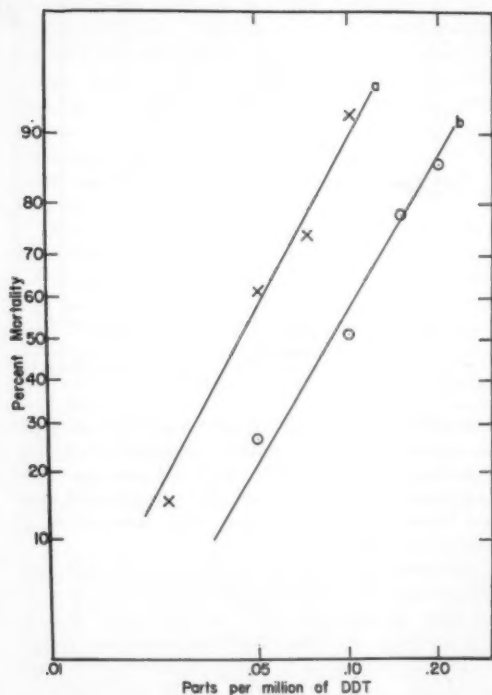


FIG. 1. Dosage-response curve of DDT as obtained with guppies (*Lebistes reticulatus* Peters).

A biological method (3) in which guppies are used as the test animal for determining the toxicity of certain insecticidal plants was modified to adapt it for detecting small amounts of DDT. Preliminary trials using technical DDT in water were made to establish the toxicity range. Five replicates of ten fish each were used at the following concentrations of DDT: 0.025, 0.050, 0.100, 0.150, and 0.200 ppm. Mortality counts, at the end of 24 hr, gave data that plotted a straight line on log probability paper (Fig. 1).

Fish from two different sources were used in these trials. Line a shows the dosage-response curve obtained with fish from a city ditch, while line b was obtained

with fish caught in a brook high in the mountains. The temperature differential in these two locations may be a factor in the observed difference in resistance. It should be noted that even though there is a significant difference in susceptibility to the poison, the lines are parallel, which indicates a similar response to varying dosages. The lower limit of sensitivity when the most susceptible fish were used was around 0.025 ppm, which concentration of DDT produced a kill of approximately 15% in 24 hr.

A practical application of this technique was made by determining DDT residues on vegetables. The experimental procedure followed was to apply a 0.1% solution of wettable DDT powder¹ (50%) to whole fresh vegetables. Four 500-g samples of both tomatoes and string beans were weighed separately into quart Mason jars. The DDT suspension was then applied from a pipette at the rates of 0, 8, 12, and 16 ppm. The samples were al-

TABLE 1
RECOVERIES OF DDT OBTAINED FROM DDT RESIDUES
ON TOMATOES AND BEANS

Samples	DDT in test solution mg/ml	Fish mortality %	DDT found mg/ml	Recovery %
Tomatoes	blank	0	—	—
	0.040	16	0.035	87.4
	.060	56	.059	98.4
	.080	92	.092	115.0
Beans	blank	0	—	—
	.040	20	.038	95.0
	.060	42	.050	83.4
	.080	74	.070	87.4
Standards* (Controls)	blank	0	—	—
	.040	24	—	—
	.060	58	—	—
	.080	84	—	—

* Standard test solutions of DDT were prepared from an acetone extract of 50% DDT wettable powder.

lowed to stand for 1 hr and then extracted using the technique described by Wichmann *et al.* (4). Acetone was substituted for benzene in this extraction procedure, as benzene is toxic to the fish. The acetone extracts were then evaporated to 100 ml so that the concentrations of the test solutions would be 0.00, 0.04, 0.06, and 0.08 mg/ml, respectively, assuming that no losses occurred in the extraction procedure. These solutions were tested on the fish, and the results obtained are presented in Table 1. The results show good recoveries for all concentrations of DDT in both vegetables, with an error within limits of biological methods.

The high sensitivity of the fish to DDT suggested the application of this biological test in detecting traces of DDT in milk. However, when diluted milk contaminated with DDT was used as the test medium, erratic results were obtained. The milk fat in some way slowed down the rate of penetration or poisoning action of DDT. This necessitated extending the exposure time to 48 hr, with the results that the controls had a high mortality.

¹ Chipman DDT (50%) spray powder.

The inconsistent results obtained with prolonged exposure in milk indicated that some factor other than the DDT was also toxic to the fish. This was substantiated by the fact that on occasions when mortality in the controls was low, the kill obtained in treated samples was proportional to the concentration of DDT. Bacteriostatic and surface-active agents, aeration, and homogenization were of no benefit in producing consistent results.

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Tyrosinase in Human Skin: Demonstration of Its Presence and of Its Role in Human Melanin Formation

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The mechanism of formation of melanin in human skin has been the subject of extensive investigation and vigorous controversy for the past 50 years (14). In 1895, Bourquelot and Bertrand (5) found in the mushroom an enzyme called tyrosinase, which catalyzed oxidation of the amino acid tyrosine to melanin. A few years later, tyrosinase was demonstrated in many plant, insect, fungus, and marine animal tissues. At this time, it was assumed that tyrosinase was also present in mammalian skin and that this enzyme catalyzed the oxidation of tyrosine to melanin. Although there was some experimental evidence to support this view, skepticism concerning the presence of tyrosinase in mammalian skin arose when reports demonstrating tyrosinase in rabbitskin could not be confirmed.

Bloch and his co-workers (4) found that on incubation of sections of human skin in a solution containing dihydroxyphenyl-L-alanine (dopa), under appropriate conditions, black granules were deposited in the melanoblasts of the basal layer of the skin. This process was shown to involve the enzymatic oxidation of dopa to melanin. The investigators (4) found that incubation of skin with compounds other than dopa, for example tyrosine and epinephrine, did not result in formation of melanin in the melanoblasts. Therefore, Bloch concluded that the melanoblasts in human skin contained a specific "dopa oxidase" which could catalyze the oxidation of dopa only to melanin.

¹Abbridgment portion of a thesis submitted by Dr. Fitzpatrick to the faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in dermatology and syphilology.

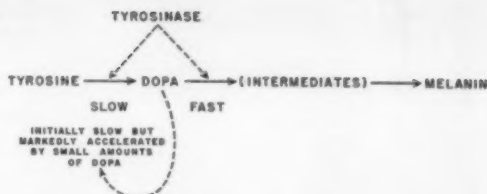


FIG. 1. Enzymatic oxidation of tyrosine to melanin by mammalian tyrosinase.

Several years later, Raper (17) showed that dopa was the first product formed in the enzymatic oxidation of tyrosine to melanin by tyrosinase of plant and insect sources. He also demonstrated that plant and insect tyrosinases could catalyze the oxidation of dopa, as well as of tyrosine, to melanin; that is, plant and insect tyrosinase possesses tyrosinase and dopa-oxidase activities.

In the past 8 years, it has been demonstrated that extracts from melanomas of mice (9, 11, 15), horses (7), and human beings (10) display both tyrosinase and dopa-oxidase activities. Furthermore, it has been shown (15) that, under certain conditions, a true distinction cannot be made between tyrosinase and dopa-oxidase activities in mammalian tissue. It was recommended (15) that the term tyrosinase be used for this enzymatic activity, instead of the separate terms tyrosinase and dopa oxidase. Dopa was also found to be a catalyst in the enzymatic oxidation of tyrosine (15). This concept is diagrammed in Fig. 1. If the view represented in Fig. 1 is correct, as opposed to Bloch's hypothesis, it should be possible, under appropriate conditions, to demonstrate tyrosinase activity in human skin. The experimental results demonstrating the presence of tyrosinase activity in human skin form the basis of this report.

It has been reported (3) that under certain stimuli—for example, ultraviolet or roentgen rays—the human dendritic melanoblasts enlarge, become branched, and give a more pronounced dopa-oxidase reaction than when unirradiated skin is used. For this reason we performed experiments in which we used nonpigmented skin of normal individuals, which had been irradiated for 8 days with erythema doses of ultraviolet radiant energy obtained from a quartz mercury vapor lamp.² The results presented in this paper represent a study of the skin (normal before irradiation) of 30 human volunteers.

On the 8th day, a specimen for biopsy was taken, by means of a punch, from the irradiated site and was fixed immediately in 10% solution of formalin for 1 hr at 5° C. Slices of the fixed tissue, 1–2 mm thick, were placed in 25 ml of 0.005 M L-tyrosine made up in 0.1 M phosphate buffer at pH 6.8³ where they remained for 24 hr at 5° C. The slices of tissue were then immersed in fresh tyrosine-phosphate buffer again, and were left in

² Alpine Sun Lamp, Luxor Model, Hanovia Chemical and Mfg. Co., Newark, N. J.

³This value is the optimal pH for the mammalian tyrosinase-tyrosinase reaction (15). There was no change in the intensity of the reaction between pH 6.8 and 7.38.

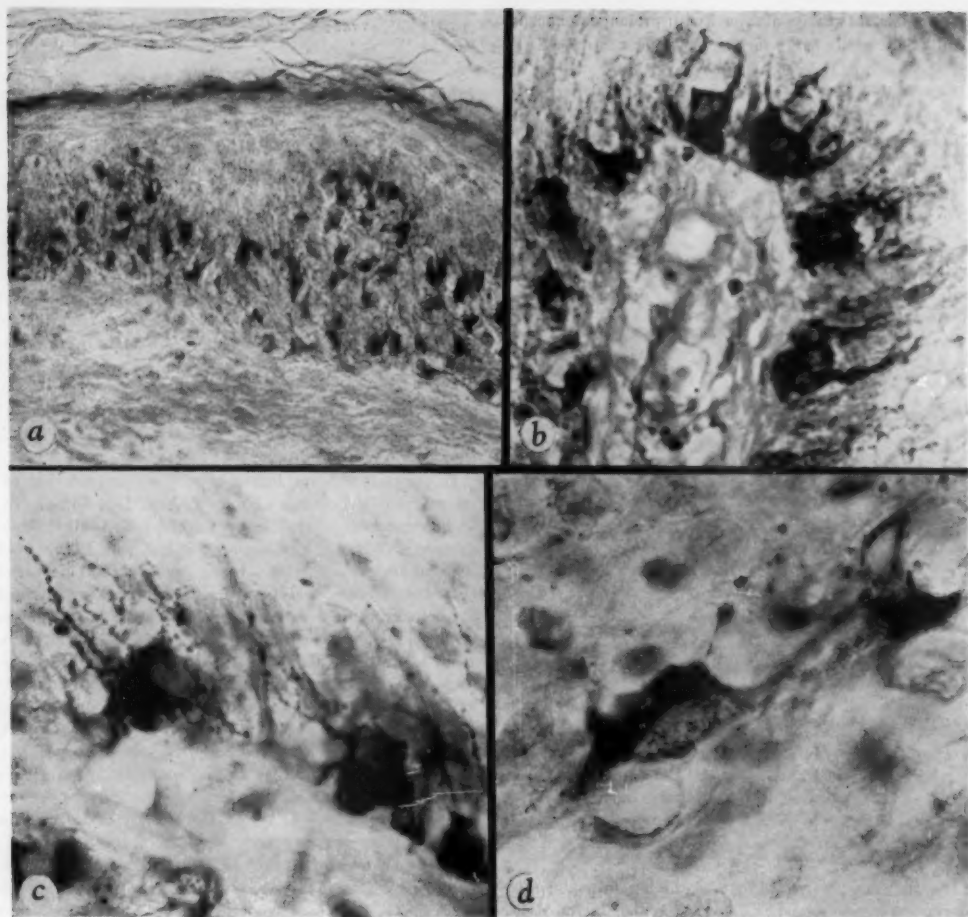


FIG. 2. Pigmented dendritic melanoblasts in human skin which has been exposed *in vivo* to ultraviolet radiant energy and incubated in tyrosine phosphate buffer. (Paraffin sections. Magnifications: a, $\times 375$; b, $\times 700$; c, $\times 1,025$; d, $\times 1,450$.)

an incubator at 37°C for another 24 hr. For one control, slices of irradiated skin were treated identically as has been described, except that phosphate buffer (without tyrosine) was used. For a second control, slices of unirradiated skin (from the same donor) were treated exactly as the first control. Gross examination of the slices of skin at this time revealed darkening of the epidermis in the slices incubated in tyrosine but no change in color in the control slices. To prepare the tissues for histologic examination, further fixation was carried out by immersing the slices of tissue in Bouin's solution (picroformal) for 24 hr; then they were dehydrated, cleared in toluene, imbedded in paraffin, sectioned at $15\ \mu$, and counterstained with borax carmine.

Fig. 2 illustrates pigmented melanoblasts lying deeply in the basal cell layer at the epidermal-dermal junction.

The outline of the melanoblast, with its dendritic processes, is delineated by the presence of fine, densely packed, brown granules which are deposited in the cytoplasm of the cell body and its dendrites. The cytoplasmic distribution of melanin granules is in agreement with results obtained by differential centrifugation of extracts from the Harding-Passey mouse melanoma, which show that tyrosinase is associated with particles in the cytoplasm of the pigment-producing cells (15).

In control sections the basal cells contained preformed melanin, but there were no dendritic melanoblasts containing tyrosinase activity at the epidermal-dermal junction. Evidence of melanin formation was not observed in the basal cells of the epidermis.⁴ Whenever melanin was

⁴ The absence of melanin formation in the basal cells of the epidermis is contrary to the impression held by others and formerly by one of the authors (H. M.).

found in the basal cells of the tissue that had been incubated in tyrosine, an equal amount of melanin was found in the basal cells of the control that had been incubated in buffer alone. A similar distribution of melanin formation was seen in sections from the same specimens when dopa-phosphate buffer was used in place of tyrosine-phosphate buffer.

Heating the tissue to 100° C for 10 min completely abolished the ability of the melanoblasts to convert tyrosine to melanin.

When the irradiated slices of skin were incubated with 0.01 M sodium diethyl-dithiocarbamate for 6 hr prior to incubation with tyrosine, the reaction was completely inhibited. Sodium diethyl-dithiocarbamate has been shown (16) to inhibit the oxidation of tyrosine catalyzed by mouse melanoma tyrosinase by combining with copper, which is necessary for enzymatic activity.

The deposition of granules of melanin in the cytoplasm of the cell body and dendritic processes of melanoblasts after incubation of human skin with tyrosine solutions indicates the presence of tyrosinase activity in these cells. The oxidation of dopa to melanin is also catalyzed by the melanoblasts, since incubation of sections of human skin with dopa results in deposition of pigment in these cells. Bloch's statement that the melanoblast contained only a specific "dopa oxidase" is apparently not supported by these findings. The data support the view that tyrosine can act as a precursor of melanin in human skin.

Human epidermal tyrosinase apparently exists in an inactive or partially inhibited state in normal unirradiated skin. Under the described experimental conditions irradiation of the skin with ultraviolet radiant energy, and possibly other types of radiation (such as roentgen rays, which are known to produce clinical pigmentation), is required before human melanoblasts can convert tyrosine to melanin. The mechanism by which ultraviolet radiant energy activates the enzymatic reaction is unknown. At least two factors appear to be involved. First, trace amounts of dopa, which are known (15) to accelerate greatly the tyrosine-tyrosinase reaction, may be formed in the melanoblast or surrounding cells. The dopa may be formed by direct photochemical oxidation of tyrosine present in the tissues and then catalyze the enzymatic oxidation of tyrosine to melanin. The conversion of tyrosine to dopa by ultraviolet radiant energy in the absence of the enzyme has been demonstrated (2, 6, 18). Second, ultraviolet radiant energy may decrease the concentration of normally occurring sulfhydryl groups in the epidermis. Rothman, Fleisch, and others (8, 19) have shown that inhibition of the tyrosine-tyrosinase reaction *in vitro* by extracts of human epidermis is attributable to the presence of sulfhydryl groups. This inhibitory action was absent after irradiation of the epidermal extracts with ultraviolet radiant energy. Sulfhydryl groups inhibit tyrosinase by combining with the copper which is required for enzyme activity.

The inhibition of the human tyrosinase reaction by sodium diethyl-dithiocarbamate suggests that this enzyme, like tyrosinase in plants (12, 13), insects (1), and in mouse melanomas (16), requires copper for its activity.

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Zinc Precipitation of Plasmin

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The work of Vallée (1) on the various zinc concentrations in certain tissues has given significance to the study of the effects of low concentrations of zinc on blood proteins. During a study of plasmin activity in ulcer exudates, I noted that the activity was lower in those ulcers treated with zinc oxide. This observation suggested studying the effect of zinc on plasmin *in vitro*.

Plasmin,¹ assaying 1 unit per mg, can be completely precipitated and inactivated by small quantities of zinc. A method of obtaining this inactivation is given here.

One ml of a solution containing 30 mg of plasmin (30 units) was added to a tube containing 198 µg of ZnSO₄ · 7H₂O in 1 ml of distilled water. This represents 45 µg of ionized zinc, assuming it is all present in the ionized form. A precipitate formed that was removed from the solution by centrifugation. The supernatant was then tested for plasmin activity against gelatin in a viscometer. No activity was detected over a period of 4 hr. Varying degrees of precipitation were noted with 22.5 µg, 11.25 µg, 5.6 µg, and 2.8 µg of zinc. At 1.6 µg no precipitation was noted. Testing of the supernatants after sedimentation of the precipitates showed a loss of activity inversely propor-

¹ Supplied by Eugene Loomis, of Parke, Davis & Company Research Laboratory.

tional to the amount of precipitate that had been formed. The supernatant from the plasmin treated with 1.6 μg of zine showed the same activity as the untreated plasmin.

The experiment was repeated using homogenized egg albumin² as a substrate, and again it was found that 45 μg of ionized zine was sufficient to precipitate 30 units of plasmin, so that no activity remained in the supernatant fluid.

A zinc chloride solution was prepared so that 1 ml again contained 45 μg of zinc, and this was also effective in completely precipitating or inactivating plasmin. The precipitate was redissolved by dialyzing it against tap water for 4 hr. Plasmin activity was demonstrated in this solution, although recovery was not complete. Dialysis of plasmin against tap water results in the loss of some plasmin activity.

The technique promises to be of value in the crystallization of this enzyme.

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² Courtesy of Otto Schales.

A Simple Technique for Observing Carotid and Brachial Artery Pulse

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Various methods have been used in the laboratory for measurement and observation of the carotid pulse. In most cases the methods employed utilized various delicate pieces of apparatus, such as double membrane tambours and kymograph drums. In many cases irregular recordings of the carotid pulse are obtained because of inertia in the equipment used. Students rarely actually visualized the pulse they were studying.

A simple technique for visualizing the carotid pulse and the brachial pulse has been developed in this laboratory. The simple apparatus necessary, as shown in Fig. 1, consists of a test tube *A*, two graduated glass tubes (with a bore of about 1 mm) *B* and *C*, a three-holed rubber stopper, two pieces of rubber hose (about 18 in. long) *D* and *D'*, and two glass funnels *E* and *E'*. (Funnels are 1.5 in. in diameter at the mouth.) The test tube is almost completely filled with water *F*, and a few drops of methylene blue, neutral red, ink, or other coloring material are added to the water, so as to obtain a slightly colored solution. Each of the graduated glass tubes is inserted in one of the openings in the rubber stopper. The rubber stopper with tubes is inserted into the test tube. A piece of rubber hose is attached to each of the glass tubes. A funnel is then inserted into the free end of each piece of rubber hose.

When either funnel is pressed against the neck over the carotid artery, air in the tubular system is bubbled out

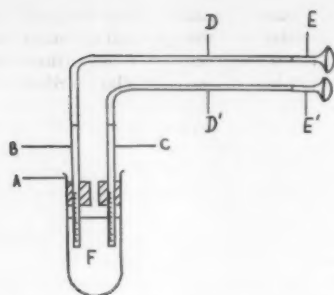


FIG. 1. Schematic drawing of apparatus used for observing carotid and brachial artery pulse.

at the submerged end. If a little more than sufficient pressure to detect carotid pulse is exerted, then slight release of pressure will draw fluid into the system to any desired height. When pressure is properly adjusted, the pulse will drive the air column through an excursion of several mm (as is noted on the graduated portions of the glass tubes).

The other funnel may be placed over the brachial artery near the bend of the elbow, and with somewhat greater pressure, the pulse in the brachial artery may be likewise observed.

If a 1-in. strip of old inner tube rubber approximately 18–24 in. long has a hole punched near its middle, through which the funnel stem is inserted, then the funnel can be held against the carotid by elastic tension, provided the tubing is drawn around the neck and fixed by means of a hemostat or clamp. A protecting roll of cloth at one side of the opposite carotid artery should be used to avoid decreased cranial flow, which may otherwise occur. It is possible that, when one funnel is thus fixed over the carotid artery, the same individual can hold the other funnel against the brachial artery. Thus the menisci of both pulse pressures can be obtained simultaneously and compared as to excursion and sequence.

Cretaceous Rocks in the Kamishak Bay Area, Cook Inlet, Alaska

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South of Kamishak Bay in the Kamishak Hills between the Kamishak and Douglas rivers, at least 2,000 feet of Cretaceous sediments rest with possible disconformity upon Upper Jurassic Naknek beds. The Cretaceous is predominantly greenish-gray, medium-grained silty current-bedded sandstone, similar in many respects to the underlying Jurassic. Near the base, bluish-gray concretionary limestone is present locally, but at other places the presumed base is marked by a thin pebble conglomerate, including well-rounded fragments of horn-

fels, volcanic rock, sandstone, granite, and fragmentary belemnites and bichias.

All fossil collections were studied by G. D. Hanna and Leo Hertlein. Middle Cretaceous fossils reported as *Lytoceras* sp., *Phylloceras* sp., and *Prionotropis* sp. were collected from the sea cliffs at the mouth of the Douglas River. Sea-cliff exposures a short distance west of the southernmost mouth of the Douglas yielded *Phylloceras* sp. Though assigned to undifferentiated Cretaceous, the latter beds are believed to be stratigraphically close to the base of the Cretaceous of the Kamishak Bay area; better collections might establish the presence of Lower Cretaceous. Collections made high in the Kamishak Hills about 7 miles southeast of the mouth of the Kamishak River include the following Upper Cretaceous genera: *Parapachydiscus*, *Phylloceras*, *Turritites*, and *Inoceramus*.

Stratigraphic relations are uncertain between the Cretaceous at Kamishak Bay and the Lower (Albian) Cretaceous at Kaguyak, 30-35 miles south. At Kaguyak, Lower (Albian) Cretaceous fossils were collected a few hundred feet above the top of the Upper Jurassic Naknek formation.

Lower Cretaceous Rocks at Cape Kaguyak North of Kukak Bay, Alaska

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Beds of Lower Cretaceous (Albian) age occur at Cape Kaguyak on the western side of Shelikof Strait about 17 miles north of Kukak Bay. Cape Kaguyak is a flat-topped promontory separated from the main coast to the west by a half-mile wide swampy sand flat. About 400 feet of beds comprising fossiliferous, concretionary, black limy siltstone with thin beds of dark bluish-gray limestone are exposed in the seacliffs on the cape and in the surrounding reefs. The presumed base of the Cretaceous is a 30-foot greenish-gray, fine-grained sandstone cropping out at the mainland edge of the sandflat west of the cape. The nature of the intervening section is unknown. The basal sandstone rests with apparent conformity on the Upper Jurassic Naknek formation. North of Cape Kaguyak along the coast west of Swikshak Lagoon a thick section of bedded rocks is exposed. Regional relations indicate that this section includes the Naknek formation at its base, overlain by beds correlative with those at Cape Kaguyak, and the section may extend upward into the Tertiary. Atwood reported Cretaceous rocks in this vicinity (1, Pl. VI).

S. W. Muller reports the following Lower Cretaceous (Albian) forms from Cape Kaguyak: *Cleoniceras* sp., *Hamites* several species, *Beudanticeras* sp., *Phylloceras* sp.

Correlation between the Kaguyak Cretaceous and the Middle and Upper Cretaceous in the Kamishak Bay region 30-35 miles north is uncertain. Lower Cretaceous rocks in the Alaska Peninsula are known at Herendeen Bay and Port Moller (1, Pl. VIII).

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Measurement of Ion Migration on Paper in an Electric Field. Transference Numbers of Nickel and Copper Sulfates

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While studying the separation of various organic and inorganic compounds of biochemical interest, a method was devised which yielded good results in some cases, and appeared to be of great promise in others. As far as the authors are aware, the method described here has not been reported previously.¹ Essentially, it is based on electrophoresis, in which a strip of filter paper serves as a path along which ions or charged particles migrate under the influence of a potential gradient.

The apparatus is illustrated in Fig. 1. A strip of filter paper,² P, 35-50 cm in length, was supported in a glass tube 2.5 cm in diam by means of two glass pins, B, piercing the paper strip and passing into small holes in the rubber stoppers at each end of the tube. The electrode vessels, A, fitted with platinum-wire electrodes, were filled with 0.1 N KCl and connected by means of an agar saltbridge with the large buffer vessels, D. The ends of the paper strip were then permitted to become completely wetted with the KCl solution by wick

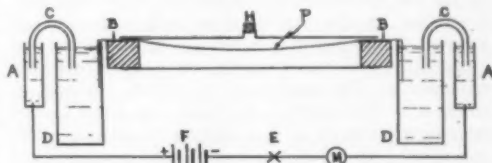


FIG. 1. Apparatus devised to study ion mobilities.

action. In certain experiments, particularly those with amino acids and proteins, solutions of electrolytes that acted as buffers were used to wet the paper strip. With the switch, E, closed, the circuit was completed. With a voltage of 135 v, provided by the batteries, F, a current of 1-3 ma was registered on the milliammeter, M.

Despite the superficial resemblance to paper chromatography, the method is basically electrophoretic in nature. Chromatographic processes depend on a distribution of some material between a mobile and a non-mobile phase. In the technique described, the separa-

¹ After this manuscript had been submitted for publication, an abstract by E. L. Durrum (1), which appears to embody some of the ideas of this paper, came to the attention of the authors.

² Eaton and Dikeman Paper No. 613 in rolled strip form, 8 mm wide.

TABLE 1
ION MOBILITIES AND TRANSFERENCE NUMBERS FOR NICKEL AND COPPER SULFATE

(+) Ion migration	(-) Ion migration	Transference number	Time	Voltage per cm	(+) Ion mobility	(-) Ion mobility
(mm)	(mm)		(sec)		$\mu/\text{sec}/\text{v}/\text{cm}$	
Nickel sulfate						
139.0	185.0	0.429	2.16×10^4	2.31	2.79	3.71
96.0	128.5	0.428	1.44×10^4	2.31	2.89	3.87
88.5	118.0	0.428	1.44×10^4	2.31	2.66	3.55
Copper sulfate						
62.5	101.0	0.382	1.44×10^4	2.31	1.88	3.04
67.5	113.0	0.373	1.44×10^4	2.25	2.03	3.40

tion results from the movement of oppositely charged ions or particles under the influence of a unidirectional potential gradient, rather than from distribution equilibria, adsorption-desorption effects, or countercurrent processes. The filter paper strip serves to hold the solvent or dispersion medium and to fix the migrating species in position when the current is turned off, thus preventing back diffusion. It is suggested that the term *ionography* be used to describe the technique.

The material to be studied was made up in a 0.038 M solution, and 0.045 ml of the solution was placed on the dampened paper strip midway between the electrodes by inserting a micropipette through opening, *H*. The initial substances whose ion mobilities were determined were nickel and copper sulfate. Under the influence of the potential, the positively and negatively charged ions migrated to opposite ends of the paper. In the case of such typical electrolytes, the circuit was opened after 3-6 hr and the paper dried.

The position of the ions on the paper was determined by the use of colorimetric reagents. Nickel ions were determined by spraying the paper with 0.1% dimethyl glyoxime in water-alcohol solution. The cupric ion was identified by the use of a 2% solution of potassium ferrocyanide. The position of the sulfate ion was determined by first spraying the paper with 0.1 M barium chloride followed by 0.1% potassium rhodizonate. The area covered by the sulfate ions remains uncolored, and the surrounding area turns red. The ion mobilities and transference numbers of nickel and copper sulfate are shown in Table 1.

The transference numbers of the ions of an electrolyte may vary with the concentration of the electrolyte. Except for the postulation of intermediate or complex ions, the mobility of a given ion depends not only on its nature and on the temperature, but also on the ionic strength of the solution, since the interionic forces have a considerable effect on the mobilities of the ions. These effects are, in general, different for the two kinds of ions of the electrolyte, and hence will give rise to transference numbers that vary with the concentration.

In the case of copper sulfate, the transference number of the cupric ion, as determined by the Hittorf method, increases from 0.327 at 0.5 N to 0.375 at 0.05 N (3). The values are in agreement with those determined previously. The transference numbers reported

here correspond to values obtained in very dilute solution by the Hittorf method, or to values computed from such data obtained at higher concentrations and extrapolated to lower concentrations.

The transference number of nickel in nickel sulfate has been reported to be 0.366 at 40° C in 0.1 N solution (2). The average value of 0.428 reported in this investigation is, therefore, not unreasonable as a limiting value, as the concentration of the salt approaches great dilution.

The endosmotic movement of the water itself will affect the movement of the ions to some extent. It would be expected that, in general, movement of the cations would be increased, while that of the anions would be retarded. That the effect is not a serious one is apparent from the relatively good agreement between transference numbers obtained by ionography and those obtained by the more time-consuming Hittorf method.

With inorganic ions, the leading edge of the ion bands was always quite sharp, but the trailing edge appeared to be rather diffuse. Preliminary experiments with inorganic ions seem to indicate that optimal separation can be secured when the paper strip is wetted with 0.1 N KCl. The purpose of the glass tube enclosing the paper strip is to maintain equilibrium between the moisture in the paper and in the environment. Usually a drop or two of the KCl solution was put into the glass tube to help establish this equilibrium.

Preliminary experiments indicate that the isoelectric point of proteins can be determined, and that amino acids and proteins can be separated by ionography. A number of complicating factors so affect the results, however, that further exploratory work is required to put these particular measurements on a sound basis. Even in the presence of a buffer in the solution, enough electrolysis takes place to cause a marked change in pH in the electrode vessels when the separate buffer vessels are omitted. This change in pH results in a change in charge on the amino acids or proteins with a consequent reversal in direction of movement part way through an experiment.

Indications are that amino acids and perhaps lower molecular weight proteins can be fractionated. A possible advantage over traditional electrophoresis techniques is that, in principle at least, it seems possible that complete separation of the constituent fractions of amino acid mixtures, or lower molecular weight pro-

teins can be achieved. This opens up the possibility of using the technique for preparative purposes, since that portion of the paper strip containing a particular fraction can be cut out and the fraction eluted by customary methods.

The fact that convection currents are of no great consequence in ionography will permit liquids other than water to be used. When electrophoretic measurements in water are made at any temperature other than in the neighborhood of 4° C, the point of maximum density, convection currents offer a serious difficulty. As very few nonaqueous liquids or liquid mixtures exhibit points of maximum density, the study of electrophoresis in the past has been restricted largely to water solutions or suspensions. In the technique described here, the elimination of convection currents means that electrophoretic studies can be extended to many organic liquids and to solutions of water with other liquids; this possibility has important implications in biochemical work, where many materials of great interest are soluble in water to only a very limited extent.

Experiments are contemplated—using sheets of filter paper instead of paper ribbon—in which the movement of charged particles or ions would be influenced not only by an electrical field but by a superimposed magnetic field as well. In effect, this system would be equivalent to a mass spectrograph applicable to charged particles in solution.

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Penetration of Benzpyrene into the Stomach Wall of Mouse

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Under what conditions and by which routes the carcinogenic hydrocarbons enter the living organism in general, and the individual cells expressly, are still almost unexplained questions.

Seeking an answer, we, among others, have painted the skin of newborn mice with carcinogen solutions and have found that the carcinogen will penetrate the epidermis directly, even though the pilosebaceous apparatus is still undeveloped and penetration through the follicular openings thus cannot take place (13). It was of interest to investigate whether other organs that come into contact with carcinogenic hydrocarbons will also absorb them. Particular attention was directed toward the alimentary canal.

In our experiments we have tried to use chemically well-defined solvents for the carcinogenic hydrocarbons,

especially those that are able to dissolve both water- and lipid-soluble substances. We have, for example, used water-soluble polyethylene glycols (Carbowaxes) as carriers for the carcinogenic hydrocarbons in our experiments (7-11, 13, 14). The hydrocarbons dissolved in these compounds penetrate easily into the skin and induce cutaneous tumors. Carbowaxes in aqueous solutions are also suitable carriers for carcinogenic hydrocarbons—for subcutaneous injections, for instance.

The so-called association colloids furnished another type of both water- and lipid-soluble solvents. These have the ability to bring carcinogenic hydrocarbons into clear and stable aqueous solutions (1, 2). Aqueous solutions of carcinogenic hydrocarbons will also induce cutaneous tumors (3, 4, 12), and tumors in the mouse forestomach (5), even when comparatively small quantities of the carcinogen are used.

The present communication deals with the penetration of benzpyrene, dissolved in Carbowax 1500, into the stomach wall of mice. The fluorescent microscope technique was used.

The animals used, about 75 in all, were adult mice of an anonymous, known strain employed for several years in our experiments on chemical carcinogenesis. 3:4-Benzpyrene dissolved in water-soluble Carbowax 1500 was introduced directly into the stomach of the animals by means of a stomach tube. The animals were killed immediately or 2-60 min or 24 hr after the application. The stomach (with or without preceding fixation in 10% neutral formalin solution) was cut on the freezing microtome at 10- μ thickness, and examined immediately with the fluorescent microscope (type Reichert Lux UV with a Philora-lamp HPW 125 w). Other specimens were embedded in paraffin in the usual manner and stained using the hematoxylin-van Gieson technique. Some unstained preparations were cut without prior application of the fluorescent substance. The concentration of 3:4-benzpyrene was 0.5%. (The investigative technique will be presented later in detail.)

The following results are reported:

Forestomach: Immediately after the application of benzpyrene in Carbowax 1500, the superficial keratinized layers showed a brilliant, almost dazzling, white fluorescence. All layers of the stratified squamous epithelium below these had taken up material with a strong blue fluorescence. The intensity of the fluorescence was much stronger than that seen in skin painted with the same solution. The fluorescent material was localized diffusely in the cytoplasm of all cells in all layers of the epithelium. Only the nuclei appeared optically empty. In other words, benzpyrene in this carrier immediately penetrates into the wall of the mouse forestomach (Fig. 1).

In addition, a strong blue fluorescence could be observed, almost without exception, in the region of both the circular and the longitudinal muscle layers of the forestomach. It was found that the fluorescent substance in this region of the stomach was gathered into a kind of fine network, which could be beautifully visualized with the fluorescent microscope (Fig. 1). We have not attempted to prove that this network of channels which



FIG. 1. Unstained frozen section from the wall of the mouse forestomach photographed in ultraviolet light. The keratinized layers, as well as the stratified epithelium, are strongly fluorescent (upper part of figure). In the muscle layer a network of fine channels contains material with blue to blue-violet fluorescence (lower part of figure).

contained strongly fluorescent material is actually a part of the lymphatic system, but it probably is. The very fine and well-developed network of channels, partly parallel and anastomosing, begins "rootlike" at the interface between the subepithelial loose connective tissue and the individual circular muscle bundles, and then runs plexiform toward the longitudinal muscle layers, and extends into the fine, longitudinal channels in this part of the stomach wall (Fig. 1). The network of these (probably lymphatic) channels extended continuously through the whole stomach—i.e., this fine system with strongly fluorescent material was well developed also in the glandular part of the stomach, as well as in the small intestine (at least in the upper segment). The mechanism of drainage of the fluorescent material via the channels mentioned above does not seem to have been observed previously.

Glandular stomach: When the preparations were made immediately after the introduction of the carcinogen dissolved in Carbowax 1500, the following could be observed: Although there is a so-called ridge at the boundary of the nonglandular and glandular part of the mucous membrane (at which the stratified cornified squamous epithelium sharply changes into glandular tissue), there did not seem to be great differences in the ability of cells in these two parts to take up fluorescent material. On the contrary, the gland cells had taken up large amounts of blue fluorescent substance in their cytoplasm. The nuclei were devoid of this material. The epithelial gland cells containing mucine had also taken up fluores-

cent material. The intensity of the fluorescence was sometimes as strong as that in the squamous-celled epithelium of the forestomach (Fig. 2).

Also, in this part of the mouse stomach, the (lymphatic) channels contained blue fluorescent material, and even the finest ones could be plainly observed under the fluorescent microscope.

The entrance and localization of the carcinogenic hydrocarbon (or its fluorescent metabolites) in the glandular part of the mouse stomach have not been established earlier with certainty. We have, however, found that benzpyrene dissolved in the water-soluble Carbowax 1500 (which is both water- and lipid-soluble) immediately enters also the cells of the glandular stomach. Not only are the cells of the upper third of the tubules able to take up fluorescent material, but also the cells of the middle third (and sometimes the cells of the lower third) take it up in their cytoplasm. The lacteals also contained—at least to some extent—the fluorescent substance.

We have thus found that 3 : 4-benzpyrene dissolved in the water-soluble polyethylene glycol (Carbowax) very rapidly enters the cells of all segments of the mouse stomach—i.e., the wall of the forestomach as well as that of the glandular stomach, penetrating the "protective mucous barrier" of the latter. In addition, it (or its fluorescent metabolites) rapidly passes through the mucous membrane into a system, most probably lymphatic, of fine channels in the outer layers of the gastric wall. Apparently the drainage via the channels presented above then takes care of the elimination of this fluorescent material. It has thus been possible to observe directly how a substance introduced into the stomach of mice is drained by this system. The existence of the especially well-developed and rich drainage system in the wall of the mouse forestomach seems to mean that this segment of the digestive canal may play a certain role in the gastrointestinal absorption.

Certain investigations concerning tumor induction in the mouse glandular stomach, planned along the new prin-



FIG. 2. Unstained frozen section from the wall of the glandular part of the mouse stomach photographed in ultraviolet light. Gland cells had taken up great amounts of strongly fluorescent material. Nuclei are optically empty.

ciples, are now in progress. The results here reported are preliminary to a report on a more detailed study of the significance of certain factors in experimental chemical carcinogenesis with carcinogenic hydrocarbons carried out since 1945 (6), as well as on the so-called solvent effect for chemical carcinogenesis in general.

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Oxygen Consumption and Radiophosphate Uptake by Minced Brain from Mice of Different Ages in Relation to Propagation of Mouse Encephalomyelitis Virus¹

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It has been reported previously (2) that brain minces from mice up to 9 days of age are capable of supporting the growth of Theiler's GD VII strain of mouse encephalomyelitis virus when cultured in a simple medium containing only salts and glucose; brains from mice 1-2 days of age yield more virus than brains from mice 3-9 days old. No evidence of virus propagation was obtained with brains of mice 10 days old or more. In this study, we investigated the oxygen consumption and radiophosphate uptake of control and virus-infected brain minces from mice of different ages in an effort to determine whether metabolic differences might be associated with the inability of older tissues to support virus propagation.

The methods employed were described in detail in

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² Predoctoral Public Health Fellow of the National Institutes of Health.

TABLE 1
OXYGEN CONSUMPTION BY MINCED BRAIN FROM MICE
OF DIFFERENT AGES

Mouse age	No. of expts.	Virus present	Q _{O₂} *				Titer after 24 hr†
			Initial	5 hr	12 hr	24 hr	
1 Day	10	-	90-110	60-80	40-60	30-40	-
	10	+	90-110	60-80	40-60	30-40	10 ⁻²
3 Weeks	3	-	130-170	60-90	10-30	0	-
	3	+	130-170	60-90	10-30	0	10 ⁻²
Adult	4	-	180-220	40-60	0	0	-
	4	+	180-220	40-60	0	0	10 ⁻²

* Values of Q_{O₂} are expressed as μ l O₂/hr/100-mg wet weight and show the ranges for the different experiments.

† The highest tenfold dilution that killed at least half of a group of 7 mice when 0.03 ml was injected intracerebrally. A titer of 10⁻² represents only survival of the original virus added.

previous papers (3, 4). Minced brain tissue (40-60 mg) was aseptically removed from mice of various ages and added to Warburg vessels or to 50-ml Erlenmeyer flasks containing 2.5 ml of Simms' solution. The pH was adjusted to 9 with dilute NaOH. Cultures were inoculated with virus or control supernatants and brought to a final volume of 3 ml with Simms' solution. Warburg experiments on oxygen consumption were carried out at 35° C with continuous shaking in an atmosphere of air. P³² uptake experiments were carried out at 35° C in stoppered, 50-ml Erlenmeyer flasks without shaking and in an atmosphere of air. At the termination of the incubation period all preparations were tested for sterility, and the virus titer was determined by intracerebral injection in mice with serial dilutions as previously described.

Oxygen consumption was measured on control and virus-infected tissues using the direct method of Warburg as previously described (3).

The results of experiments with minced brain from 1-day-old mice, 3-week-old mice, and adult mice are given in Table 1. The initial metabolic rate is distinctly higher in 3-week-old and in adult mouse brain than in the 1-day-old group. However, the metabolism of the older tissue declines much more rapidly with time than does that of 1-day-old brain minces. As was previously noted (3), the presence of the virus had no influence on oxygen consumption of the 1-day-old mouse brain, although the virus was shown to propagate rapidly in this tissue. No virus propagation was observed in 3-week-old or adult mouse brain.

Studies were made of the uptake of radioactive orthophosphate into the organic acid-soluble (OAS) fraction, the phospholipid (LP) fraction, and the "total protein-bound" (TPP) fraction by the procedures previously described (4). The chemical analysis for P³² was carried out by a modification of the method of Fiske and Subbarow (1) in which ascorbate was used as a reducing agent and a heating period was employed for color development and stabilization. Radioactive samples were prepared in ¼-oz tin ointment dishes, and

TABLE 2

P^{32} UPTAKE INTO THE OAS, LP, AND TPP PHOSPHATE FRACTIONS OF MINCED MOUSE BRAIN OF VARIOUS AGES INCUBATED 24 HR IN THE PRESENCE AND ABSENCE OF VIRUS

Mouse age, days	Relative specific activity*						Virus† titer
	OAS		LP		TPP		
	No virus	Virus	No virus	Virus	No virus	Virus	
1	53.5	51.7	2.9	4.2	2.4	3.5	10 ⁻³
	47.6	50.8	3.0	4.1	2.3	3.5	
7	22.2	30.2	2.0	2.2	1.2	1.5	10 ⁻⁴
	26.0	24.3	1.9	2.2	1.3	1.6	
10	19.4	24.8	1.2	1.2	0.9	0.9	10 ⁻³
	21.3	24.2	1.4	1.4	0.9	0.9	
14	26.0	24.8	0.8	0.8	0.7	0.7	10 ⁻³
	23.0	24.7	0.8	0.8	0.7	0.7	
23	19.6	20.1	0.6	0.6	0.6	0.6	10 ⁻³
	18.5	17.4	0.6	0.6	0.6	0.6	

* Relative specific activity = $\frac{\text{counts}/\mu\text{g } P^{32} \text{ in the fraction}}{\text{counts}/\mu\text{g } P^{32} \text{ in IP fraction}} \times 100$.

† A titer of 10^{-3} represents the initial virus inoculum and corresponds to survival only.

counted with a thin, mica-window Geiger-Müller counter tube. A minimum of 3,000 counts per sample was taken.

Table 2 gives data for the uptake of P^{32} in a 24-hr incubation period into the OAS, LP, and TPP fractions of virus-infected and noninfected minced brain from 1-, 7-, 10-, 14-, and 23-day-old mice. Values are expressed as relative specific activities, i.e., the specific activity of the fraction relative to the specific activity of the inorganic phosphate fraction (IP). It is apparent that the incorporation of P^{32} into the lipid and protein-bound fractions was most extensive in the 1-day-old minced mouse brain, and was less extensive as tissue from older mice was employed.

The previously noted stimulation of P^{32} uptake by virus infection of minced 1-day-old mouse brain (4) is apparent in the experiments reported in Table 1. A definite but smaller stimulation is apparent in the 7-day-old mouse brain. P^{32} uptake by brain from mice older than 7 days did not show stimulation by virus infection. Stimulation of P^{32} uptake by virus infection is seen to correspond to the propagation of the virus. No difference between the phosphorus distribution in the control and infected cultures was noted, although there was the expected increase in the total lipid and protein phosphorus in older tissue (Table 3).

The initial rate of oxygen consumption of minced brain from 1-day-old mice is considerably lower than tissue from 3-week-old or adult mice. The 1-day-old tissue, however, can maintain its oxygen consumption

TABLE 3

DISTRIBUTION OF PHOSPHORUS IN THE VARIOUS FRACTIONS OF MINCED MOUSE BRAINS OF DIFFERENT AGES INCUBATED 24 HR IN THE PRESENCE AND ABSENCE OF VIRUS

Mouse age, days	Micrograms of phosphorus per 100 mg wet tissue					
	OAS		LP		TPP	
	No virus	Virus	No virus	Virus	No virus	Virus
1	25	31	44	48	45	46
	24	25	47	43	44	45
7	26	30	55	55	43	45
	28	24	56	58	45	44
10	30	26	54	53	48	49
	25	24	52	51	49	47
23	30	25	64	60	57	53
	28	29	61	60	55	56

for long periods in a culture medium containing only salts and glucose, whereas the Q_{O_2} of tissue from older mice declines much more rapidly. The propagation of Treiler's GD VII virus in minces of 1-day-old mouse brain did not affect the rate of oxygen consumption.

In a 24-hr incubation period, the minced brain tissue from 1-day-old mice was found to incorporate radioactive phosphate into the tissue lipides and proteins more extensively than the tissue from older mice. The virus did not grow in minced brain cultures from mice older than 9 days and exerted a stimulatory effect on the uptake of P^{32} into the lipides and proteins only in those young cultures in which virus propagation could be demonstrated. The data suggest that the ability of 1-day-old minced mouse brain cultures to permit the propagation of the virus is associated with the ability of this tissue to maintain its oxidative metabolism over a sufficiently long period to allow virus multiplication. Most virus production appears to occur in the period from 12 to 24 hr (2).

The difference in the ability of 1-day-old mouse brain and of older mouse brain to support the propagation of Theiler's GD VII virus *in vitro* may be associated with the greater ability of the younger mouse brain to maintain oxidative or glycolytic metabolism for long periods of time. This hypothesis would resolve discrepancies and explain the observation that the intact adult mouse develops paralysis in spite of the failure to demonstrate virus propagation *in vitro* in adult brains.

References

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2. PEARSON, H. E. *J. Immunol.*, to be published.
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4. RAPELSON, M. E., JR., WINZLER, R. J., and PEARSON, H. E. *J. Biol. Chem.*, 1949, 131, 583.

Comments and Communications

The Study of Disordered Systems

The communication of A. G. Huntsman with regard to "Scientific Research vs. the Theory of Probabilities" (*Science*, 1949, 110, 566) is interesting indeed, though the subject discussed there is in need of a more complete exposition than he has provided. It is certainly true, in a sense, that mathematicians have gained a great deal of prestige, often even in the eyes of the biological scientists that Dr. Huntsman represents, but it is greatly to be questioned that this is entirely the result of their being able to command something like mystified awe from their admirers rather than that they have been able many times to light a way through problems that would have remained inscrutable without their help.

There is certainly no need to justify the construction of a concept of perfect disorder for the purpose of dealing with some of the problems of modern physics and chemistry, or to justify the development of probability theory as a branch of pure mathematics. The results speak for themselves. To compare the states of physics before and after Maxwell, or of the theory of errors before and after such mathematicians as Khintchine and Kolmogoroff, is to be convinced that indeterminability, i.e., ignorance, can be dealt with in precise terms, and the process made to yield intelligible and useful results. However, in the science of biology, which does not yet share either the philosophical attitudes of the other natural sciences (see, for example, the confused atmosphere of du Noüy's *Human Destiny*) or their ability to manipulate their problems symbolically and thus to maintain a nice balance between the experimental and theoretical parts of investigation, it is still an acceptable habitus to be frightened by the strange world of mathematical operations, seeing in them only complexity where there is really preciseness and simplicity.

It may be epigrammatic to say that the theory of probability permits the exact systematization of ignorance, but it is also quite misleading. By means of a particular calculus, the theory of probability, or the theory of random processes, disordered systems can be specified with the same degree of precision as ordered systems; it is simply obscuring the intent of this viewpoint to erect the dichotomy "ordered systems vs. disordered systems equals knowledge vs. ignorance." The conclusion that actuarial tables are useless because they are unable to predict the day on which a particular person will die is based upon a failure to recognize the restrictions that the theory of probability has freely and necessarily placed upon itself. It is sufficient to observe here that the insurance companies continue to earn money in spite of these difficulties. In yielding generalities of steadily increasing inclusiveness, consistent with the results of experimentation, as it has so eminently done, the study of disordered systems has written its own *raison d'être*.

It is the belief of the writer that the mistrust of a statistical viewpoint (and to some extent the mistrust of mathematics as a tool in biology) arises not so much from the difficulties involved in replacing an older notion of a one-to-one correspondence between cause and effect, or even of causality itself, with one of chance determination of events, as rather from the difficulty of erasing entirely the older notion of causality and not attempting to replace it with any equivalent idea, counting ourselves lucky to have removed a barrier to intellectual and scientific progress. In fact, it might almost be said that the concept of causality itself is a sort of philosophic dodge, a symbol without a referent, a semantic chimaera that has seated itself so firmly in our intellectual tradition that it can now be dislodged only with great difficulty.

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The inadequate logic of A. G. Huntsman's argument embodied in his letter "Scientific Research vs. the Theory of Probabilities" (*Science*, 1949, 110, 566) will be obvious to all those who have had even an elementary training in the applications of probability in scientific research, but for the benefit of beginners it may be advisable to point these out. The principle of his criticism seems to be that statistical laws with reference to populations are of no scientific value because they do not accurately predict what will happen to any particular individual. This amazing statement is supported by two examples—Dr. Huntsman was himself refused life insurance over twenty years ago, and a friend of his was accepted for life insurance in the morning and died going upstairs in the afternoon. Anyone in his right senses who wishes to know how long he can expect to live, will consult his doctor rather than a life insurance table. The life insurance company is not concerned with the individual as such, but only with what will happen to the population as a whole. Is the conclusion respecting the population, which is of acknowledged accuracy, any less scientific because it does not concern itself with the future of a particular individual?

Dr. Huntsman expresses a basic objection to the use of probability methods. To quote from his letter:

The biologist's greatest gift from mathematics might well be, not a theory that may delude him into belief that he is wise when he is ignorant, but rather the ideal of clear definition and precise use of his terms and symbols, not excepting science and research.

It is clear, again, that a statistical law stating a characteristic of a population as a whole is regarded as ignorance merely because it fails to make an accurate statement with respect to a particular individual, and the poor biologist or physicist is deluded by the mathema-

tician into thinking he is wise when he is really ignorant. This statement sets one to wondering who is really ignorant. Can it be that there are leading biologists in Canada who are not aware of the tremendous progress made in recent years in the fields of physics, physical chemistry, and applied mathematics, wherein the laws discovered are essentially statistical in that they deal with the average behavior of units of matter and fail completely to describe or predict the behavior of an individual unit? To take a very familiar example, laws have been discovered dealing with the natural disintegration of radioactive materials. By means of these laws the half-life of a piece of radium can be accurately predicted, but no physicist can point to an individual atom and make any prediction as to when it will disintegrate. Possibly all knowledge of fundamental things must be expressed eventually in terms of probability. In this field scientists are coming closer and closer to a knowledge of the ultimate. As they approach this end they can be assured by Dr. Huntsman that they will be approaching the acme of total ignorance.

In biology the application of mathematical methods and in particular probability methods is indeed increasing. Biologists are delving into fields of research where variability exists, and in order to derive order out of chaos they must deal with population trends rather than the behavior of an individual toad, say, which may or may not be characteristic of the population to which it belongs. I take violent objection to Dr. Huntsman's statement that "there is an increasing tendency to force use of the theory of probabilities upon those engaged in scientific research." There are still a great many problems to be solved in those fields where results are often clear-cut and obvious, and there is no quarrel with those who wish to stay in this narrow field and content themselves with the solution of problems of this type, but the more advanced thinkers should not be retarded in their development by such superficial criticism of their mode of action. The entomologist wants to know what happens to a given population of insects when a predator moves in. Is it not rather childish to say that he is not being scientific unless he wants to know what will happen to a particular insect? The plant pathologist is concerned with the balance between populations of plants and disease organisms. All the preliminary and more elementary phases of the relation between the plant and the organism under given conditions have probably been worked out, but this still does not provide the answer to the question as to what will happen in nature.

Predictions of a statistical nature about populations as a whole may be of much greater importance than those concerned with individuals. Even in the human field it

is clear that accurate predictions with respect to a given individual (actually impossible because of difficulty of predicting his future environment) are of far less value to the human race, than predictions dealing with the population as a whole. Whether or not such prediction methods are worthy subjects of scientific research, or merely an acknowledgment of ignorance, can very easily be left to the discretion of the average research worker.

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May I, at this late date, be allowed to comment on A. G. Huntsman's letter (*Science*, 1949, 110, 566), which has only now come to my notice? It will be limited comment, confined to those parts I understand, because some parts, for instance the statement "The prestige of mathematics is so great that many persons forget that even in mathematical hands, probability, chance, and random mean ignorance," are on a semantic plane beyond my reach.

However, I take it that the nub of Dr. Huntsman's plaint is this: That the use of the theory of probability to handle aggregates blinds the researcher to his proper task of investigating the behavior of individuals. Perhaps the best rejoinder is simply that studies of aggregates and individuals are complementary. This notion is indeed an implicit *sine qua non* of the work of all good scientists—including those who, like Dr. Huntsman, outwardly assert that it involves an antilogy. Was Clerk Maxwell wrong to develop the kinetic theory of gases before a thorough investigation of molecular behavior had been carried out? Does the solvency of life insurance companies inhibit medical research in diagnosis and prognosis? Is the zoologist working on a rat contributing more to the corpus of scientific knowledge than the epidemiologist working on the correlation between rat population and typhus? These are the kinds of questions to be mulled over by Dr. Huntsman and anyone who shares his views.

Finally, it is to be remembered that the distinction between aggregates and individuals is in some respects a convenient fiction. If we abandon the study of disease statistics in favor of the study of single cases, so might we abandon the study of what the pathological organisms cause en masse in a particular case in favor of the study of individual organisms. Now, organisms contain aggregates of cells, cells of molecules, molecules of atoms. . . . I seem to recall a rhyme about big fleas and little fleas—composed, be it noted, by a mathematician.

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Book Reviews

Medical Physics, Vol. II. Otto Glasser, Ed. Chicago: Year Book Publ., 1950. 1,227 pp. \$25.00.

This monumental volume lists 181 contributors, who include many of the most distinguished contributors to medical physics and its related fields. Volume II supplements Volume I, which contained 1,792 pages and sells for \$20.00; the two volumes can be purchased together for \$40.00. Subjects treated only in Volume I are listed by title in Volume II.

A striking feature of the new volume is the numerous articles dealing with radiation. Atomic energy has nowhere had greater impact than in questions of health. Thus, for one who is concerned with protection against radiation, two articles by Karl Z. Morgan and Carl B. Braestrup give full accounts of monitoring and protection methods. Austin M. Brues describes the symptoms of radiation sickness and its therapy. A fuller account of radiation therapy is given by H. E. Johns. Still other aspects of this field are treated by Gustav Bucky, Edith H. Quimby, and W. E. Forsythe with E. Q. Adams. Even these articles are but a fraction of the papers devoted to radiation.

As one looks through the titles, starting with "Accelerators: High-Energy," by M. Stanley Livingston, and ending with "Weighing," by A. A. Benedetti-Pichler, one discovers that many subjects have been treated in the first volume and are not repeated in Volume II. There is thus a very real reason for considering the purchase of the two volumes at the reduced price. The books are expensive, but they are well printed, the subjects cover the medical field well and are generally excellent. The bibliographies are extensive. Anyone interested in understanding the scientific side of medical physics should have access to both volumes.

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Microbiologie du Sol: Problèmes et Méthodes. S. Winogradsky. Paris: Masson et Cie, 1949. 861 pp. 3,000 fr.

In this volume Winogradsky has arranged and edited his publications in microbiology. The purpose of the edition is twofold: first, to gather in one volume the contributions otherwise available only in widely scattered journals; the second, more important, is best told in the author's words:

Pour ma part, ce qui m'incite à entreprendre la reconstitution de toute une vie de recherches scientifiques c'est l'idée que cette chronique, analysée et commentée par son auteur lui-même à la fin de sa carrière, pourrait bien être utile aux débutants dans ce genre d'études. Au lieu de faits établis, terriblement nombreux et d'importance inégale . . . ils pourront y trouver un tableau vivant, en quelque sorte, de la recherche microbiologique avec ses méthodes changeantes, adaptées au but à atteindre, ses succès et ses déboires, et cela sur des problèmes qui figurent au premier plan des

recherches microbiologiques depuis leur début et jusqu'au temps présent, donc au cours de plus d'un demi-siècle.

Only Winogradsky could trace from firsthand experience the important developments in soil microbiology from 1885 up to the present.

The papers have been arranged in ten groups, with an appropriate foreword, written in 1945, that places each in its proper setting. Articles originally published in other languages have been translated into French, with the exception of two in English. Numerous typographical errors and some repetition of material slightly impede the presentation, but in most parts of the book these go unnoticed as the ideas unfold.

In the first section are expressed the viewpoints, maintained almost unchanged throughout the author's career, which led to so many fundamental discoveries. The most important of these was that microbes and their activities must be studied as they occur in nature, with methods appropriate to this end. The inadequacies of the classic procedures for studying the sulfur bacteria are pointed out, and a new microculture method permitting continuous microscopic observation is described. With it, the experiments leading to an understanding of the metabolism of the sulfur bacteria, the first-known autotrophs, were performed. This was an epochal event in biology. The discovery of autotrophic metabolism was in a sense a by-product of the study of the morphology of the sulfur bacteria under natural conditions, and well illustrates the validity of the Winogradsky axiom that microbes must be studied as they live in nature.

The culture of the sulfur bacteria having been worked out, the classic studies on their morphology were completed. The results routed from its last stronghold the concept of microbial pleomorphism as a ready transformation of bacteria of one kind into another. Pleomorphism as later revived by Löhnis is also vigorously assailed by Winogradsky. This section provides a discussion of the fundamental aspects of microbial morphology that should be read by every microbiologist.

The third section includes the conclusive experiments which proved the autotrophic nature of the nitrifying bacteria. The method that was finally developed for isolating and studying them is described in detail.

It is interesting that in seeking free-living nitrogen-fixing bacteria Winogradsky found the anaerobic forms rather than *Azotobacter*. The isolation and ecology of *Clostridium pasteurianum* are described in section 4 and also mentioned in section 8. Experiments on the retting of flax (section 5) are given in the short space of 5 pages.

Between 1906 and 1922 Winogradsky was prevented from continuing his investigations, but in 1922 he was invited by Roux to accept a position with the Pasteur Institute as head of soil microbiology. In this capacity he devised techniques which would give more accurate information on the activities of microbes in the soil. The direct method was perfected (this method is not limited

to soils) and is described in section 6. In the direct method soil is maintained under conditions similar to those in the field, and the microbial types which develop on added substrates are identified by direct microscopic examination and subsequent culture. This technique was used to show the importance of the cytophagas in the aerobic decomposition of cellulose in soil (section 7) and to demonstrate that *Azotobacter* is by far the most significant fixer of nitrogen (section 8).

The production of ammonia by *Azotobacter* is discussed at length. Numerous experiments, intended to prove that it is a product of nitrogen fixation rather than autolysis, are described. Although by modern biochemical standards the data and experimental techniques do not establish conclusively that N_2 is reduced directly to ammonia, the results do show that ammonia is given off from the cells under conditions simulating those in nature.

Data on ammonia production by nodules of legumes are presented in section 9, with results essentially similar to those found with *Azotobacter*. The concluding section formulates some principles of microbial ecology.

The keen analysis of fundamental problems and the simple and successful methods used to solve them mark Winogradsky as one of the world's greatest masters of microbiology. All microbiologists, but particularly beginners in soil microbiology, should be greatly indebted to him for this edition, which fully realizes the purpose of the author. His work has already profoundly influenced the ideas and practices of innumerable scientists, and its ready availability in *Microbiologie du Sol* assures that this influence will continue.

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Scientific Book Register

- The Cerebral Cortex of Man: A Clinical Study of Localization of Function.* Wilder Penfield and Theodore Rasmussen. New York: Macmillan, 1950. 248 pp. \$6.50.
- Metallurgical Applications of the Electron Microscope.* London, England: Institute of Metals, 1950. 164 pp. \$3.50.
- Soviet Psychiatry.* Joseph Wortis. Baltimore, Md.: Williams & Wilkins, 1950. 314 pp. \$5.00.
- Inorganic Syntheses*, Vol. III. Ludwig F. Audrieth, Ed. New York: McGraw-Hill, 1950. 230 pp. \$3.75.
- Electromagnetic Theory*, Vols. I, II and III. Oliver Heaviside. New York: Dover Publs., 1950. 386 pp. \$7.50.
- Handbook of Physiology & Biochemistry.* 40th ed. R. J. S. McDowall. London: John Murray; Philadelphia: Blakiston, 1950. 767 pp. \$7.00.
- Principles of Genetics.* 4th ed. Edmund W. Sinnott, L. C. Dunn and Th. Dobzhansky. New York: McGraw-Hill, 1950. 505 pp. \$5.00.
- Electricity and Magnetism: Theory and Applications.* 3rd ed. Norman E. Gilbert. New York: Macmillan, 1950. 569 pp. \$5.00.
- Heat and Temperature Measurement.* 2nd ed. Robert L. Weber. New York: Prentice-Hall, 1950. 422 pp. \$6.65.
- Some Theory of Sampling.* William Edwards Deming. New York: John Wiley; London: Chapman & Hall, 1950. 602 pp. \$9.00.
- Elements of Ordinary Differential Equations.* Michael Golomb and Merrill Shanks. New York: McGraw-Hill, 1950. 356 pp. \$3.50.

Association Affairs

Salt Lake City Meeting of the Pacific Division

The 31st annual meeting of the Pacific Division, AAAS, was held in Salt Lake City, June 19-24, at the invitation of the University of Utah. The university, which this year is celebrating its one-hundredth anniversary, offered a most cordial and hospitable welcome and provided unusually fine facilities for the meeting. The Student Union Building, which served as registration headquarters, provided a cafeteria and coffee shop, rooms for group luncheons and banquets, committee rooms, and meeting rooms for part of the scientific sessions. General sessions were held in Kingsbury Hall, which has a seating capacity of 2,000. Other sessions were held in conveniently located university buildings. The physical arrangements contributed markedly to a successful, well-integrated meeting.

The divisional symposium held on Tuesday morning—"The Westward Migration and Its Consequences"—was

of outstanding interest and importance. Four papers were presented: "Westward Ho! America Moves West," by Leland H. Creer, professor of history, University of Utah; "Population Pressure and Its Impact on the Environment," by John Tee-Van, of the Conservation Foundation and the New York Zoological Society; "Land Use, the Basis of Western Economy," by Sigmund V. Wantrup, professor of agricultural economics, University of California; and "Forestry Practice and Watershed Management, the Key to Resource Conservation," by Reed W. Bailey, director of the Intermountain Forest and Range Experiment Station. Presentation of these papers was followed by lively discussion.

This symposium was followed by an address on Tuesday evening by Olaus J. Murie, president of the Wilderness Society, on "Saving the Western Wilderness."

On Tuesday afternoon the president of the University of Utah, Albert Ray Olpin, and Mrs. Olpin, received

members and guests of the Pacific Division and associated societies at the president's home.

The address of Laurence M. Klauber, retiring president of the Pacific Division, was given Wednesday evening. His subject was "Rattlesnakes and Man." Dr. Klauber, an electrical engineer whose avocation is herpetology, not only provided a large amount of information about rattlesnakes, but cited numerous myths and legends about them.

On Thursday evening Albert Cage, president of the California Electric Power Company, Riverside, California, spoke on "Artificial Rainmaking on a Western Watershed," detailing three years of successful experience in increasing precipitation by seeding supercooled clouds with dry ice. Mr. Cage emphasized that the success of the undertaking was due to the special conditions prevailing in the area in question, where clouds sweep up across the crest of the Sierra and are likely to dissipate eastward without producing any precipitation unless artificially activated.

On Friday evening Ralph E. Wilson, of the Mount Wilson Observatory, presented "The Story of Palomar," a motion picture, followed by slides of the latest pictures taken with the 200-inch telescope.

The presence of Roger Adams, the national president, and Raymond L. Taylor, assistant administrative secretary of the AAAS was greatly appreciated. Both of these officers informally addressed the Council of the Pacific Division at its meeting on Wednesday afternoon.

Twenty of the societies associated or affiliated with the Pacific Division participated in the meeting. The programs thus covered a broad field of science ranging from astronomy to bacteriology, from chemistry to soil science, and from nature study to the technical aspects of population analysis. The large number of symposia, and topical programs in which various points of view were brought to bear on a single subject, afforded evidence of careful planning by the officers and program committees of the participating societies.

For the American Society of Ichthyologists and Herpetologists this was a national meeting which, owing to its central location, was unusually well attended by members from all parts of the country. Although the geographical location might have seemed to favor herpetology, there was an abundance of papers on fishes, both fresh-water and marine. Two of the sessions for reading of scientific papers, and the annual dinner, were held in conjunction with the Herpetologists League.

All of the local committees functioned smoothly and effectively under the able chairmanship of I. Owen Horsfall, director of University Extension. Much credit is due him and his capable staff for the efficient handling of the many details incident to the successful organization and management of the meeting. Thomas J. Parmley was chairman of the Committee on Reception and Entertainment, and Mrs. Parmley was chairman of the Committee on Women's Activities. The activities of these two committees were admirably coordinated. No one was left with time on his hands but had, instead, to make a choice among several desirable alternatives.

A high light of the joint activities of these committees

was the special organ recital on Monday evening in the Salt Lake Tabernacle, with a lecture by Alexander Schreiner, tabernacle organist, on "Sound in Organ Pipes." This unusual evening of entertainment was made possible through the cordial cooperation of ecclesiastical administrators of the Salt Lake Tabernacle.

Admirably conducted trips were provided to the famous Bingham Copper Mine, Great Salt Lake, and Brighton, with its thrilling ski lift at the head of Big Cottonwood Canyon—Salt Lake City's beautiful year-round resort.

Charles H. Danforth, professor emeritus of anatomy, Stanford University, was elected president of the Pacific Division for the ensuing year, and Robert C. Miller, director of the California Academy of Sciences, was reelected secretary-treasurer. Vincent P. Gianella, professor of geology, University of Nevada, was elected a member of the Executive Committee; Sarah R. Atsatt, University of California, Los Angeles, and James Bonner, California Institute of Technology, were elected to membership on the Divisional Council.

It was decided by unanimous vote to accept the invitation of the University of Southern California to hold the next annual meeting on its campus in Los Angeles, June 18-23, 1951.

Attendance at the Salt Lake City meeting included 760 registered members and guests, representing a wide geographical area, as indicated by the following tabulation:

GEOGRAPHIC DISTRIBUTION OF REGISTRANTS

Arizona	7	Nevada	7
California	258	New Jersey	4
Colorado	31	New Mexico	2
District of Columbia	7	New York	5
Florida	1	North Dakota	1
Idaho	23	Ohio	4
Illinois	4	Oklahoma	1
Iowa	3	Oregon	54
Kansas	2	Pennsylvania	6
Maine	2	Rhode Island	1
Maryland	1	South Dakota	1
Massachusetts	5	Tennessee	1
Michigan	11	Texas	5
Minnesota	2	Utah	214
Missouri	2	Virginia	1
Montana	14	Washington	71
Nebraska	1	Wyoming	8
Total, United States		740	
Australia	2	England	1
Belgium	1	Hawaii	1
British Columbia	14	Japan	1
Total, foreign or overseas		20	
Grand Total		760	

From the six states and British Columbia of the Pacific Division of the AAAS (indicated in bold face) there were 621 registrants, or 82 percent of the total registration. It is impressive that this divisional meeting of the Association attracted 126 registrants from 27 other states, 7 from the District of Columbia, and 6 from abroad. In addition to Salt Lake City—the site of the host institution, the University of Utah—there were registrants from 18 other communities in Utah.

ROBERT C. MILLER,
Secretary

Hotel Reservations and Advance Registration, Cleveland Meeting, December 26-30, 1950

As forecast earlier in the year, the 117th meeting of the American Association for the Advancement of Science, in the Public Auditorium and downtown hotels of Cleveland, December 26-30, 1950, will be full-scale. All seventeen of the Association's sections and subsections will have strong, particularly timely, and significant programs, which will include a number of important symposia. There have been recent additions to the number of societies that will hold their meetings with the Association.

The Annual Science Exposition, which will be held in the street level arena of the Public Auditorium, will be substantially larger and more diversified than was possible in the limited space available at the New York Meeting. Leading book publishers, scientific supply houses, microscope manufacturers, instrument makers, and prominent industrial concerns will have exhibits. With nearly 150 booths, the exposition will be well worth a trip to Cleveland for itself alone.

Attendance at the Cleveland Meeting will be large, and it is not too soon to be considering hotel reservations and advance registration. On separate pages in this issue will be found detailed data on Cleveland hotel accommodations. Headquarters for each section or society is shown here:

Hotel Headquarters, Cleveland Meeting

Statler:

(1,000 rooms) E. 12th St. & Euclid Ave.	AAAS; Press; AAAS Sections I, K, Q; AAAS Cooperative Committee; Academy Conferences; National Association of Biology Teachers; National Academy of Economics and Political Science, Pi Gamma Mu; American Dietetic Association; National Science Teachers Association; American Nature Study Society, National Association of Science Writers, Scientific Research Society of America, Sigma Delta Epsilon, Society of the Sigma Xi, United Chapters of Phi Beta Kappa.
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Hollenden:

(1,000 rooms) 610 Superior Ave. (E. 6th St.)	AAAS Sections F, G, N (including Subsections Nm, Nd, Np); American Society of Parasitologists, American Society of Protozoologists, American Society of Zoologists, Society of Systematic Zoology; American Microscopical Society, Society of Industrial Microbiologists; Alpha Epsilon Delta, Premedical Honor Society.
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Carter:

(600 rooms)
Prospect Ave. &
East 9th St.

AAAS Sections A, E, L, O; National Geographic Society, National Speleological Society; Biometric Society, Eastern North American Region; History of Science Society, Philosophy of Science Association; Foundation for the Study of Cycles.

Allerton:

(550 rooms)
1802 E. 13th St.

AAAS Sections B, C, D, H, M; American Meteorological Society, Oak Ridge Institute of Nuclear Studies; American Home Economics Association.

Auditorium:

(300 rooms)
E. 6th St. &
St. Clair Ave.

Particularly convenient for exhibitor personnel, since it is across the street from the Cleveland Public Auditorium.

Olmsted:

(200 rooms)
E. 9th St. &
Superior Ave.

Although sufficient rooms have been promised by the Cleveland Convention and Visitors' Bureau, it is quite probable that the supply of single rooms in the downtown hotels will become exhausted. To make it possible for all who come from out of town to be housed in the downtown, or most convenient, area, it is strongly urged that those who expect to attend will plan, from the outset, to share a room with a colleague or a friend. Most hotel rooms have space for the installation of another bed. When such rooms are sold for single occupancy, not only do they cost more, but members who do not make reservations until December may be obliged to stay in a less conveniently located hotel. Suites shared by three or four persons may cost less than the single rate, and double rather than single occupancy of individual rooms is always more economical.

Advance Registration. The advantages of receiving the General Program well in advance of the Meeting are real ones—provided the Program arrives early! To insure that all advance registrants shall receive their programs on time, programs will be mailed *first class*, December 1-4, 1950. To cover most of the postage, the advance registration fees have been increased 25¢; that is, the fees will now be \$2.25 for members of the Association, for spouses of registrants, and for bona fide college students, and \$3.25 for nonmembers. No advance registrations received after December 4 can be accepted.

News and Notes

About People

Erwin H. Amick, Jr., associate professor of chemical engineering at Columbia University, has been appointed to the new post of associate dean of the School of Engineering. Dr. Amick is now in Germany, where he is serving for the second successive summer as a technical consultant to the Department of the Army in connection with the operation of I. G. Farben Industries.

Norris E. Bradbury, director of the University of California Los Alamos Scientific Laboratory in New Mexico since 1945, has been given the additional appointment of professor of physics in the Department of Physics at Berkeley.

Woodrow E. Byrum has been appointed professor of pharmacology at the University of Georgia School of Pharmacy. Dr. Byrum has been head of the Department of Pharmacology at the School of Pharmacy, University of Arizona, for the past two years.

Carl E. Hookings, formerly of the Department of Health of the Province of Ontario, Canada, has joined the faculty of the Division of Preventive Medicine, University of Tennessee College of Medicine, as assistant professor. He will also direct the Maternal and Child Hygiene Division of the Memphis and Shelby County Health Department.

F. R. Hunter, formerly of the University of Oklahoma, and **L. M. Beidler**, formerly associated with The Johns Hopkins University, have joined the staff of the Department of Physiology at Florida State University, Tallahassee. Dr. Hunter will work in general physiology, and Dr. Beidler will work in biophysics.

Edward Mack, Jr., chairman of Ohio State University's Department of Chemistry, has been elected to the Board of Directors of the Oak Ridge Institute of Nuclear Studies. Dr. Mack was appointed to complete the

unexpired two-year term of **George B. Pegram**, former vice president of Columbia University.

W. Glenn Moss, formerly associate professor of pharmacology at Temple University School of Medicine, has been named assistant professor of physiology at the University of Illinois College of Medicine.

Paul Rosenberg has been elected president of the Institute of Navigation, New York City, for the academic year 1950-51, to succeed **Gordon McLintock**, Rear Admiral, USMS. Dr. Rosenberg will retain his position as president of Paul Rosenberg Associates, New York firm of consulting physicians.

John T. Tripp has been appointed chief of the Section on Human Blood Products, Laboratory of Biologic Control, Microbiology Institute, National Institutes of Health. Dr. Tripp, a biochemist and immunologist, was formerly assistant director of the Division of Laboratories, Michigan Department of Health, where he was in charge of the manufacture of serums and vaccines for the past 15 years.

Frank J. Veihmeyer, professor of irrigation in the University of California's College of Agriculture, Davis, has been elected president of the Hydrology Section of the American Geophysical Union for the period 1950-53. As president, Dr. Veihmeyer will be U. S. representative at the meeting of the International Geophysical Union in Belgium in 1952.

Visitors

William T. Astbury, professor of biomolecular structure, University of Leeds, England, will deliver the first Harvey Lecture of the current series at the New York Academy of Medicine on September 28. Dr. Astbury will speak on "Adventures in Molecular Biology."

Recent visitors at the Communicable Disease Center, USPHS, Atlanta, were **Otto R. Gsell**, chief physi-

cian, Medical Clinic, Kanton Hospital, St. Gallen, Switzerland; **Raul Aleo**, Department of Parasitology, Chilean Public Health Service, Santiago; **Armando M. Silva**, medical sanitarian, Secretary of Health and Assistance, Niteroi, Rio de Janeiro; **Pedro Nel Saavedra**, port sanitation doctor, Ministry of Hygiene, Bogotá, Colombia; **Bienvenido P. Caro**, medical assistant, Health Department, Manila, Philippines; and **Shinken Ohama**, president, Yaeyama Doctors' Association, Yaeyama, Okinawa.

Recent visitors at the National Bureau of Standards were **Sir Richard V. Southwell**, formerly rector, Imperial College, London; **W. G. Sutton**, professor of civil engineering, University of Witwatersrand, Johannesburg, South Africa; **Mary G. Vaisey**, assistant lecturer on mathematics, Imperial College, London; and **Goro Yoshida**, director, Electrical Communication Laboratory, Ministry of Communications, Tokyo.

Grants and Awards

The Army Medical Services has granted \$25,000 to Truman G. Blocker, Jr., professor of plastic and maxillofacial surgery, University of Texas Medical Branch, Galveston, for studies relating to thermal injury and epithelization.

The Squibb Institute for Medical Research, New Brunswick, New Jersey, has approved 32 new and renewal grants and fellowships for 1950-51, totaling \$149,460. The new grants are: **James A. Baker**, New York State Veterinary College—\$1,000 for support of the Cornell Research Laboratory for Diseases of Dogs; **Wallis E. Brown**, University of Arkansas—\$5,600 for studies in endocrinology; **Robert F. Chinack**, College of Medical Evangelists—\$925 for studies with vitamin B₁₂; **Byron B. Clark**, Tufts College—\$9,000 for studies with central nervous system drugs; **Robert E. de Alvares**, University of Washington—\$500 for

studies of anesthesia in obstetrics; *Walter Finke*, University of Rochester—\$600 for preliminary studies of treatment of bronchopulmonary infection in children; *H. O. Halvorsen*, University of Illinois—\$5,000 for studies in development of new antibiotics; *William L. Hewitt*, University of California—\$3,800 for support of a section on infectious diseases and chemotherapy at Wadsworth General Hospital; *H. Corwin Hinshaw*, Stanford University—\$1,800 for a fellowship under his direction for studies on streptomycin and dihydrostreptomycin; *Joseph W. Jailer*, Columbia University—\$2,500 for a fellowship under his direction for studies of metabolism of steroids; *William A. Jeffers*, University of Pennsylvania—\$5,000 for studies on abnormal physiology of hypertension; *Mary Karp*, Wesley Memorial Hospital—\$4,370 for studies on dihydrostreptomycin; *Seymour Lieberman*, Columbia University—\$5,000 for studies in endocrinology; *A. E. McIntyre*, University of Nebraska—\$5,500 for studies on local anesthetics; *E. K. Marshall, Jr.*, The Johns Hopkins University—\$4,120 for a fellowship under his direction for studies in endocrinology; Massachusetts General Hospital—\$10,000 for support of its research fund; *A. E. Rakoff*, Jefferson Medical College—\$2,400 for research in endocrinology; *Paul Resnikoff*, New York Hospital-Cornell Medical Center—\$2,500 for studies in hematology; *R. Plato Schwartz*, University of Rochester—\$10,000 for support of the drug program in the Orthopedic Clinic; *Robert E. Sealock*, Iowa State College—\$10,200 for studies of the chemistry and biochemistry of vitamin B₁₂; *Hirsh Sulikowitch*, Harvard Medical School—\$2,000 for development of a method for sodium assay in body fluids; *Klaus Unna*, University of Illinois—\$2,667 for studies with central nervous system drugs; *F. K. Volk*, Saginaw County Department of Health—\$1,500 for studies of evaluation of biologicals; and *Theodore von Storch*, Montefiore Hospital—\$1,200 for studies of vitamin B₁₂ and multiple sclerosis.

The Franklin L. Burr Prize of \$1,000 has been awarded by the

National Geographic Society to Frank M. Setzler, head curator of the Department of Anthropology, U. S. National Museum, in recognition of his contributions as deputy director of the recent Ethnological-Biological Expedition to Arnhem Land, Australia (*Science*, May 20, 1949, p. 528), sponsored by the society, the Smithsonian Institution, and the Australian government. A similar award was presented to Charles P. Mountford, director of the Australian Department of Information, who headed the expedition.

The American Geographical Society has made three awards "for special distinction in the field of exploration and geographical research." The Cullum Geographical Medal was awarded to Hans W. von Ahlmann, professor of geography, University of Stockholm, for his work in glacier study. The Charles P. Daly Medal was awarded to Laurence Dudley Stamp, professor of social geography, University of London, for contributions to food production in Britain and for town and rural planning. Robert Larimore Pendleton, professor of tropical soils and agriculture, The Johns Hopkins University, was awarded the David Livingstone Centenary Medal for work in the field of geography in the Southern Hemisphere.

Scholarship and Lectureship

The Section on Experimental Medicine and Therapeutics of the American Medical Association has established a lectureship in honor of George R. Minot, noted pathologist and former director of Thorndike Memorial Laboratory, Boston City Hospital, who died last February. The first lecture will be given at the 1951 meeting of the association by William B. Castle, present director of Thorndike Memorial Laboratory.

The John and Mary R. Markle Foundation, 14 Wall Street, New York, will continue for a fourth year its program of 5-year grants for Scholars in Medical Science to help young scientists interested in teaching and research to become established in academic medicine. A total of 47 scholars on the staffs of

35 medical schools in the U. S. and Canada are now being aided by these grants. Twenty were chosen in 1950. The number to be named in 1951 has not been determined.

All medical schools are invited to nominate one candidate. Grants of \$25,000, payable at the rate of \$5,000 annually, will be made to the schools over a 5-year period for the support of each scholar selected. Nominations should be made to the foundation on or before December 1.

Colleges and Universities

A new staining technique for diagnosis of skin and tissue diseases due to fungus infections has been developed in the Department of Dermatology and Syphilology in the University of Pennsylvania's School of Medicine. A laboratory test, using the Hotchkiss-McManus stain for coloring cellulose, with basic fuchsin as the final coloring substance, makes it possible for physicians to differentiate between suspected cases of cancer, tuberculosis, and syphilis, and the diseases traceable to fungi. The staining method can be applied to deep-seated fungus infections by using biopsy specimens, sputum, urine, lymph, or other effluvia, and many positive diagnoses can be made on specimens in which fungus was not shown by previous methods. The research was conducted by Albert M. Kligman, Senior Research Fellow of the U. S. Public Health Service, and Herbert Mescon, Damon Runyon Research Fellow, both members of the faculty of the university's School of Medicine.

Botanists of the University of Wisconsin are using plant tissue cultures to investigate the function of the plant hormones that control growth. Under the direction of Folke Skoog, associate professor of botany, and Cheng Tsui, the group is studying the effect of varying quantities of auxins and adenine on stem tissue grown in laboratory flasks on an artificial medium.

The University of Texas is sponsoring a joint research project with the U. S. Air Force School of Aviation Medicine, Randolph Field, Texas, which is designed to increase

the accuracy of psychological selection of flying personnel. The program will include a series of research projects dealing with psychological and physiological measurements of anxiety and anxiety reactions, and will be carried out in conjunction with the Air Force program of development of psychiatric screening tests for flyers. During the three years of the contract, a maximum of four graduate students a year from the University of Texas will be assigned as interns to the School of Aviation Medicine's Department of Clinical Psychology. Karl M. Dalenbach, chairman of the Department of Psychology, University of Texas, is director of the project for the university. Saul B. Sells, chief of the Department of Clinical Pathology, School of Aviation Medicine, is project director at that school.

Western Reserve University, Cleveland, has appointed Donald L. Thistlethwaite, assistant in philosophy and psychology at the University of California, as assistant professor of Psychology. Mathews C. Waddell, Johns Hopkins University, has been appointed assistant professor of mathematics. Additions to the faculty of the School of Medicine are: William E. Abbott, associate professor of surgery; T. George Bidder, assistant professor of pharmacology; Guilio L. Cantoni, associate professor of pharmacology; and Roger B. Scott, of Johns Hopkins University, associate professor of obstetrics and gynecology.

Industrial Laboratories

Bausch and Lomb Optical Company, Rochester, New York, is sending John V. Sharp, recent recipient of the Sherman Fairchild Award of the American Society of Photogrammetry, to Leopoldville, Africa, to work with Belgian technicians on a government-sponsored project to produce the first topographic map of the Belgian Congo. The contour maps, similar to those made by the U. S. Army Air Force during World War II, will be used to further the development of the Belgian Congo's mineral deposits—which include uranium, copper, tin, cobalt, silver, gold, and diamonds—in planning

railroads and flood control projects, and in building pipe lines.

The Metalloy Corporation, of Minneapolis, a division of the Lithium Corporation of America, is distributing the first supplement to the *Annotated Bibliography on the Use of Organolithium Compounds in Organic Synthesis*, published in January, 1949. The original publication contained abstracts from chemical journals for the period 1929-47. The supplement, containing abstracts of more than 150 papers, covers the two-year period 1948-49. It will be mailed to chemists who received the annotated bibliography. Further information concerning the abstracts may be obtained from Metalloy Corporation, Minneapolis, Minnesota.

The Research Division of the **Upjohn Company**, Kalamazoo, Michigan, has prepared two active adrenal steroids that differ from cortisone in having a hydroxyl group rather than a ketone group at the 11-position on the steroid nucleus. The two compounds, corticosterone (compound B) and 17-hydroxycorticosterone (compound F), have been supplied recently for limited clinical testing in rheumatoid arthritis and Addison's disease, but amounts available do not allow further distribution at the present time.

Smith-New York, Freeport, New York, has published a catalogue listing chemicals available in ampoules of a special design—stronger than pharmaceutical ampoules—in 5-, 10-, and 25-gram sizes. Intended primarily for corrosive liquids, the "tubules" are also being used for other chemicals. They are particularly useful to universities and industrial stockrooms. The catalogue is available on request.

Meetings

The Division of Rubber Chemistry of the **American Chemical Society** will hold its first international meeting in Cleveland, October 11-13, with headquarters at Hotel Cleveland. Rubber chemists from England, France, Italy, the Netherlands, and Germany will present 25 technical papers, and American

chemists will present an equal number in the scientific program, which will stress international exchange of information on the compounding and processing of natural and synthetic rubber. Amos W. Oakleaf, of Phillips Petroleum Company, has been named general chairman. The American Chemical Society, 60 East 42nd Street, New York City, will furnish further information about the meeting.

The **American Institute of Electrical Engineers** will hold its annual fall general meeting October 23-27, at the Skirvin Hotel, in Oklahoma City. Advances in power generation, the basic sciences, and communications—including radio and television—will be discussed at two general meetings; three days will be devoted to specific technical aspects of electrical engineering and allied fields.

The **American Public Health Association** and 32 related organizations in the field of public health and preventive medicine will hold meetings at Kiel Auditorium, St. Louis, Missouri, October 30-November 3. The Lasker Awards for 1950 and the Sedgwick Memorial Medal of the association will be presented during the meeting. Additional information may be obtained from Reginald M. Atwater, Executive Secretary, American Public Health Association, 1790 Broadway, New York City.

Deaths

Brayton Eddy, curator of insects and reptiles for the New York Zoological Society during the past five years, died July 17 at the age of 51. Dr. Eddy, a well-known entomologist, established the country's first insect zoo at Goddard Park in Providence, Rhode Island, in 1935.

Rollin G. Myers, chemist, died recently at his home in Palo Alto, California. He served as Chemist in Charge, USN, Cavite, Manila Bay, Philippine Islands, from 1929 until the base was destroyed by bombing in December, 1941. He and Mrs. Myers were prisoners of war from that time until they were rescued by American forces in the spring of

1945. Dr. Myers was 73 at the time of his death.

Vasil Obreshkove, 60, professor of biology at Bard College, Annandale-on-Hudson, New York, died at his summer home in Ellisburg, New York, July 15. Dr. Obreshkove had been on the faculty of St. Stephen's (now Bard College) for 25 years.

Wortley Fuller Budd, 73, dean emeritus of the School of Pharmacy, Medical College of Virginia, died July 26 in Richmond, Virginia. Dr. Budd was dean from 1920 until his retirement in 1947. He was awarded the Herty Medal in 1948 in recognition of his contribution to chemistry in southeastern U. S.

A revitalized Air Force physiological training program has been organized to familiarize Air Force flying personnel with the physiological stresses encountered in military aviation.

Physiological training for Air Force personnel was first established in March, 1942, because the necessity for such a program had earlier been recognized by combat commanders and flight surgeons during World War II. By 1943, this program involved the use of some 60 low-pressure chambers at 50 different Air Force bases in the U. S. and overseas. Hundreds of doctors participated in the teaching of the program, some of whom were physicians, but the majority were doctors of philosophy in physiology drawn from teaching and medical research centers. During approximately three years of operation, they trained thousands of airmen through the use of lectures, demonstrations, training films, and simulated flights in low-pressure chambers. During the summer of 1945, however, the loss of personnel occasioned by rapid demobilization resulted in the closing of nearly all the altitude training units and marked the end of the physiological training program.

In the summer of 1946, action was taken to reinstitute the program. The extreme shortage of aviation physiologists and Medical Corps officers in the service precluded their

being assigned to this program. As a solution to the problem, a group of 14 volunteer pilots, all of whom had combat flying experience, were detailed to the USAF School of Aviation Medicine, where an intensive course of training qualified them to perform the duties of instructors in the program. Since that time, an additional 9 pilots have also received this training and have been assigned as instructors to the U. S. operating units.

In the event of another war, it is to be expected that currently assigned instructor personnel will resume their duties as pilots, and plans envision the recall of reserve physiologists for duty as instructors in this program. Several reserve physiologists are now earning credits through two weeks of active duty training periods with various low-pressure chamber training units. Under the name of "The Physiological Training Program," indoctrination has now been augmented to include demonstrations of the greater hazards encountered in new type planes, such as ultrasonics, higher "G" forces, and many of the other physiological dangers introduced by modern warfare. Civilian reserve physiologists interested in participating in this program are encouraged to apply through their numbered Air Force headquarters for active duty training and/or mobilization assignments with existing or proposed physiological training units. Nonreserve civilians desiring appointment in the USAF Reserve for subsequent duty in this program should get in touch with The Surgeon General, USAF, Washington 25, D. C.

A Unesco scientific exhibit, captioned entirely in Spanish, will open at Lima, Peru, this month and then go on an extended tour of major Latin-American cities as part of the science popularization program of Unesco. The show, designed and constructed at the Massachusetts Institute of Technology, will be taken to Lima by Christina Buechner, executive secretary of the Committee on International Scientific Publications of the National Research Council and consultant to Unesco on Latin-American problems. It will demonstrate

the principles of physics and astronomy, and the work of high school science clubs.

The text of the physics section was prepared by John C. Slater, head of MIT's Physics Department. Harlow Shapley, director of the Harvard College Observatory, and C. A. Federer, Jr., editor of *Sky and Telescope*, were responsible for the astronomy portion of the show, which includes a portable planetarium operated within a domed enclosure seating 40-60 people. The science club exhibit was arranged by Science Service, of Washington, D. C., which administers the Science Clubs of America, sponsored by the Westinghouse Educational Foundation. This section was designed to stimulate the growth of similar science clubs among Latin-American youth.

Recently Received

Report of the Committee on a Treatise on Marine Ecology and Paleocology, 1948-49. Division of Geology and Geography, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

Never Too Old. New York State Joint Legislative Committee on Problems of Aging, 1949. Thomas C. Desmond, Chairman, New York State Legislative Committee on Problems of the Aging. 94 Broadway, Newburgh, New York.

Mode of Action of Organic Insecticides. Robert L. Metcalf, University of California Citrus Experiment Station. \$1.00.

Monofluoroacetic Acid and Related Compounds. Maynard B. Chenoweth, University of Michigan Medical School. 50 cents. Publications Office, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

Grasshopper Outbreaks in North Dakota, 1898-1948. Reprints on request. J. A. Munro, Department of Entomology, North Dakota Agricultural College Experiment Station, State College Station, Fargo, N. D.

Nutrition in Ophthalmology. John J. Stern. Nutrition Monograph Series, No. 1. National Vitamin Foundation, Inc., 150 Broadway, New York City.

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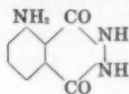
iso-Butyraldoxime (Eastman 6144) is something of a curiosity among reagents making their debut in Eastman's new List No. 37. (If you haven't received your copy, we'd like to know.) Its molecular weight of 87.12 is unusually low for a reagent of its type. It's an unpleasant-smelling liquid, four molecules of which react with a molecule of either CoCl_2 , NiCl_2 , or CuCl_2 by direct crystallization in alcohol solution to give compounds that are nonelectrolytes.

From Gallstones . . .



Bilirubin (Eastman 2101) is one of a distinguished minority of Eastman Organic Chemicals that are not synthetics. Matter of fact, we isolate it from gallstones in a battery of Soxhlet extractors that we run for days and days on end. Since the supply of gallstones is limited and since we get only a 1% yield even from black gallstones (they're the best), the purified pigment is a bit expensive. But biochemists, who use it largely as a colorimetric standard, find that a little bilirubin goes a long way.

Light-Giver . . .



3-Aminophthalhydrazide (Eastman 3606) is still one of the more spectacular items in the Eastman list. Also called "luminol," it is probably the most efficient of chemiluminescent substances. A dilute aqueous alkaline solution, with hydrogen peroxide and another common oxidizing agent like potassium ferricyanide, gives a prodigious display of "cold light." Long a sure-fire lecture demonstration, it's the basis of numerous schemes by which science outshines the firefly. But that's only half the story. Back in the middle '30s, W. Specht at the University of Jena found that 3-aminophthalhydrazide has the eerie property of causing blood stains (the older the better) to glow brilliantly enough to be photographed in the dark. It even works on bushes, on rusty fences, in soapy water, and is said to detect as little as five drops of blood dissolved in six quarts of water.

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INTRODUCTORY NUCLEAR PHYSICS

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By REYNOLD C. FUSON, *University of Illinois*. This is the first and only book at an advanced level to present the fundamental knowledge, both theoretical and descriptive, that all organic chemists must possess. The organization of the book places emphasis on the reactions of organic compounds, correlating them with one another. Theories, analogies, contrasts, discontinuities, and empirical rules are employed to a great extent to aid in assimilating and mastering the facts. Ready in September. Approx. 628 pages. \$8.00.

STATISTICAL DECISION FUNCTIONS

By ABRAHAM WALD, *Columbia University*. Written under the sponsorship of the Office of Naval Research, this book presents the foundations of statistical decision functions—a comparatively recent development in general theory. *Statistical Decision Functions* provides the principles for multi-stage experimentation, and includes the general multidecision problem. The latter treats the important question of deciding with minimum risk which of several alternative decisions is best. One of the Wiley Publications in Statistics, Walter A. Shewhart, Editor. August 1950. 179 pages. \$5.00.

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2. You receive the General Program early in December in ample time, unhurriedly to decide among the events and the sessions that you wish to attend.
3. Your name and hotel address will be in the enlarged Visible Directory the first hour of the first day of the meetings, since it will be posted in Washington as soon as processed.
4. Advance Registrants will have the same privileges of receiving a map and directory of points of interest of Cleveland, literature, radio broadcast tickets, etc. At the convenience of Advance Registrants, these will be distributed from the Main Registration in the Public Auditorium—the location of the Annual Science Exposition, the Visible Directory, and the Science Theatre. Admission to the splendid series of latest scientific films will be free to all Registrants.

At the 1949 Meeting, the Council of the AAAS voted overwhelmingly to continue Advance Registration. To insure its prompt receipt, the General Program will be sent by *first class mail* December 1-4, 1950—which is also the *closing date* for Advance Registration.

----- **THIS IS YOUR ADVANCE REGISTRATION COUPON** -----

1. Advance Registration Fee (the extra quarter covers part of the first class postage) enclosed:
☐ \$2.25 A.A.A.S. Member (check one) ☐ \$2.25 College Student
☐ \$2.25 Wife (or Husband) of Registrant ☐ \$3.25 Nonmember of A.A.A.S.
2. FULL NAME (Miss, Mrs., Dr., etc.)
(Please print or typewrite) (Last) (First) (Initial)
3. ACADEMIC, PROFESSIONAL, OR
BUSINESS CONNECTION
4. OFFICE OR HOME ADDRESS
(For receipt of Program and Badge)
5. YOUR FIELD OF INTEREST
6. CONVENTION ADDRESS
(If not known now may be added later)
7. DATE OF ARRIVAL DATE OF DEPARTURE

Please mail this Coupon and your check or money order for the fee, \$2.25 or \$3.25, to
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE
1515 Massachusetts Avenue, N.W., Washington 5, D. C.

HOTEL RESERVATIONS

117th AAAS MEETING

Cleveland, December 26-30, 1950

The list of hotels and the reservation coupon below are for your convenience in making your hotel room reservation in Cleveland. Please send your application, *not* to any hotel directly, but to the Housing Bureau of the Cleveland Convention and Visitors' Bureau to avoid delay and confusion. The experienced Housing Bureau will make assignments promptly and the hotel will send a confirmation directly to you in two weeks or less. **Please plan to share a room with a colleague.** In addition to economy, this will insure ample accommodations for all in the *downtown* hotels. Mail your application *now* to secure your first choice of desired accommodations.

HOTELS AND RATES PER DAY

Hotel*	Single	Double	Twin-Bedded	Suites
STATLER	\$4.00-\$8.00	\$7.00-\$10.00	\$8.50-\$12.50	\$17.00-\$23.00
HOLLENDEN	\$3.50-\$8.00	\$5.50-\$10.00	\$7.00-\$12.00	\$12.00-\$22.00
CARTER	\$4.00-\$6.50	\$6.00-\$10.00	\$7.00-\$10.00	\$18.00-\$25.00
ALLERTON	\$3.50-\$7.00 \$2.50 RW	\$6.00-\$ 9.00	\$6.00-\$10.00 \$4.00 RW	\$10.00-\$20.00
AUDITORIUM	\$3.50-\$5.00	\$5.50-\$ 7.50	\$7.50	\$12.50-\$26.00
OLMSTED	\$3.00-\$6.00	\$5.00-\$ 9.50	\$7.00-\$ 9.50	\$10.00-\$15.00

Prices are subject to change, but are not likely to do so.

RW means running water only—no private bath.

* A list of the headquarters of each society and section is under **Association Affairs, SCIENCE**, August 25 and in **THE SCIENTIFIC MONTHLY** for September.

THIS IS YOUR HOTEL RESERVATION COUPON

Mrs. Louise D. Perkins, Director
Housing Bureau
Cleveland Convention and Visitors' Bureau, Inc.
511 Terminal Tower
Cleveland 13, Ohio

Date of Application

Please reserve the following accommodations for the 117th Annual Meeting of the AAAS:

TYPE OF ACCOMMODATION DESIRED

Twin-Bedded..... Rate.....
Suite..... Rate..... Number in Party.....
Double Room..... Rate.....
Single Room..... Rate..... Sharing this room will be:
.....persons

(Enumerate and attach list giving name and address of each person, including yourself)

CHOICE OF HOTEL

First Choice..... Second Choice..... Third Choice.....

DATE OF ARRIVAL..... DEPARTURE DATE.....

(These must be indicated)

SIGNED.....

(Please print or type)

ADDRESS.....

(Street)

(City and Zone)

(State)

Mail this now to the Housing Bureau.

Rooms will be assigned and confirmed in order of receipt of reservation.

Hotels will confirm directly in two weeks or less.

Personnel Placement

CHARGES and REQUIREMENTS for "PERSONNEL PLACEMENT" Ads

1. Rate: 15¢ per word, minimum charge \$3.00 for each insertion. If desired, a "Box Number" will be supplied, so that replies can be directed to SCIENCE for immediate forwarding. Such service counts as 8 words (e.g., a 25-word ad, plus a "Box Number", equals 33 words). All ads will be set in regular, uniform style, without display; the first word, only, in bold face type.

For display ads, using type larger or of a different style than the uniform settings, enclosed with separate border rules, the rate is \$16.00 per inch; no extra charge for "Box Numbers".

2. Advance Payment: All Personnel Placement ads, classified or display, must be accompanied by correct remittance, made payable to SCIENCE. Insertion can not be made until payment is received.

3. Closing Date: Advertisements must be received by SCIENCE, 1515 Mass. Ave., N.W., Washington 5, D. C., together with advance remittance, positively not later than 14 days preceding date of publication (Friday of every week).

POSITIONS WANTED

Academic Position with research is desired by Ph.D., age 32, with extensive experience in endocrinology, organic structure and synthesis, growth factors, respiration and proteins; assistant professor of biochemistry; publications. Box 281, SCIENCE. X

Chemist: M.A., woman, 23. Two years teaching as graduate assistant; experience as literature chemist, analyst. Desires college or technical school teaching or analytical research position. Box 269, SCIENCE. 8/25

Entomologist; Ph.D.; four years instructor in general entomology, medical entomology, parasitology, eastern university; past nine years on faculty university medical school teaching medical entomology to medical and graduate students. For further data, including bibliography and information regarding research, please write Burneice Larson, The Medical Bureau, Palmolive Building, Chicago. X

Geographer-geologist, Ph.D., 40, veteran, desires college teaching position. Experienced college teacher, strong backgrounds in meteorology and electronics, can teach physics. Numerous publications. Prefer western states. Available immediately. Box 270, SCIENCE. 8/25

Organic chemist, Ph.D.; seeks teaching appointment; nine years' teaching experience, including four years as head of department. For further data, please write Burneice Larson, Medical Bureau, Palmolive Building, Chicago. X

Ph.D. with experience in research, teaching, editorial and information service, abstracting and translating available for research academic, research, or consulting work, especially in the field of agricultural chemicals. Box 280, SCIENCE. X

Physiologist; M.S.; Broad background in biology; 2 years teaching, research experience; research interests center about circulation; prefer academic position. Box 279, SCIENCE. X

Plant Pathologist. Excellent research and teaching qualifications. Desires position with university or research organization. Ph.D. fall 1950. Box 282, SCIENCE. X

POSITIONS OPEN

Physicists, mathematicians, mechanical engineers, electronics engineers: Cornell Aeronautical Laboratory, an affiliate of Cornell University, has permanent positions open for men of project engineer caliber with advanced degrees and experience in physics, applied mathematics, instrument design, and electronics. Assignments are varied and professionally challenging in fields of pure and applied physics. The position of our laboratory is between those of universities and commercial research institutes. We believe it combines many of the traditional advantages of both. Inquiries will be treated as confidential; they should be addressed to Mr. Nathaniel Stimson, Department T, Cornell Aeronautical Laboratory, Inc., P.O. Box 235, Buffalo 21, New York. 9/8

Personnel Placement

POSITIONS OPEN

Position Open—Physiology: Assistant Professor of Physiology, Medical Faculty. Apply to: H. G. Grant, Dean, The Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada. X

Positions Open:

(a) Biochemist, Ph.D., with sound knowledge of bacteriology; to serve as assistant director of research, pharmaceutical company. (b) Mycologist; department of parasitology, university medical school; young physician interested in teaching, research required. (c) Physiologist; department of physiology, large university; new extensive research laboratories concerned principally with human physiology; rank dependent upon qualifications. (d) Medical director; pharmaceutical company; duties include developing new products, clinical research. (e) Physician or Ph.D., trained in vascular-renal physiology; research appointment; university medical school; Midwest. (f) Ph.D., Sc.D., or M.D. in medical entomology; research dealing with malaria and entomological aspects of tropical diseases; Africa. (g) Bacteriologist, Ph.D.; to direct graduate program in bacteriology, college for men, 7000 students. SS-4 Burneice Larson, Medical Bureau, Palmolive Building, Chicago. X

Scientists: Salaried positions, \$3,600 to \$25,000. This confidential service for outstanding men who desire a change of connection, will develop and conduct preliminary negotiations without risk to present position. Send name and address for details. Tomsett Associates, 1205 Berger Building, Pittsburgh 19, Pa. H

Technical Editor: For weekly scientific publication. \$4,000-\$5,000 per year, depending on background and experience. Box 273, SCIENCE. 8/25

The Market Place

CHARGES and REQUIREMENTS for "MARKET PLACE" Ads

1. Rate: 20¢ per word for classified ads, minimum charge \$5.00 for each insertion. Such ads are set in uniform style, without display; the first word, only, in bold face type. For display ads, using type larger or of a different style than the uniform classified settings, and entirely enclosed with separate rules, rates are as follows:

Single insertion	\$16.00 per inch
7 times in 1 year	14.50 per inch
13 times in 1 year	13.00 per inch
26 times in 1 year	11.50 per inch
52 times in 1 year	10.00 per inch

2. Payment: For all classified ads, payment in advance is required, before insertion can be made. Such advance remittances should be made payable to SCIENCE, and forwarded with advertising "copy" instructions.

For display advertisers, monthly invoices will be sent on a charge account basis—providing satisfactory credit is established.

3. Closing Date: Classified advertisements must be received by SCIENCE, 1515 Massachusetts Avenue, N.W., Washington 5, D. C., together with advance remittance, positively not later than 14 days preceding date of publication (Friday of every week).

For proof service on display ads complete "copy" instructions must reach the publication offices of SCIENCE, 1515 Massachusetts Avenue, N.W., Washington 5, D. C., not later than 4 weeks preceding date of publication.

BOOKS

WANTED TO PURCHASE:
SCIENTIFIC PERIODICALS
Sets and runs, foreign and domestic
SCIENTIFIC BOOKS
Entire libraries and smaller collections
WALTER J. JOHNSON
125 East 23rd Street, New York 10, N. Y.

The Market Place

BOOKS

WANTED — YOUR PERIODICALS

We need Complete Sets, Runs, Volumes and Single numbers.
CASH IN on your periodical accumulations NOW!
COLLEGE LIBRARY SERVICE • Dept. A, Box 311, N. Y. 3
Also send us your list of wants

Send us your Lists of
SCIENTIFIC BOOKS AND PERIODICALS
which you have for sale.
Complete libraries; sets and runs; and single titles are wanted.
Also please send us your want lists.
STECHERT-HAFNER, INC., 31 East 10th Street, New York 3.

Your sets and files of scientific journals
are needed by our library and institutional customers. Please send
us lists and description of periodical files you are willing to sell
at high market prices. J. S. CANNER AND COMPANY, 909
Boylston Street, Boston 15, Massachusetts.

SUPPLIES AND EQUIPMENT

... for MORE SALES

TELL ... YOUR SALES STORY to the more than 33,000 SCI-
ENCE subscribers ... a fertile market for your Scientific
Books, Services, or Supplies.
and ... this same responsive audience, as evidenced by the
increasing number of regular "Market Place" advertisers.
SELL ... PROOF that SCIENCE advertising produces results!

Send your ad copy NOW — for the October 6, 1950 "Annual Equip-
ment Issue" featuring the latest developments in scientific in-
struments and equipment. It's an all-important issue for ad-
vertisers, as evidenced by the 1949 issue which carried 40
pages of ads.

See "Charges and Requirements" page 14,
or write for Rate Card 26 today.

LABORATORY ANIMALS

Clean healthy well-fed animals
• Guaranteed suitable for your needs.
Reasonably priced—Dependable service

DOGS RATS RABBITS
CATS PIGEONS HAMSTERS
MICE POULTRY GUINEA PIGS
JOHN C. LANDIS • Hagerstown, Md.

ANIMAL CAGES AND ACCESSORY EQUIPMENT

ORDERS NOW ACCEPTED FOR EARLY DELIVERY
HOELTGE BROS., Inc.
1919 Gest St. Cincinnati 4, Ohio
Write for New 1950 Catalog

• HYPOPHYSECTOMIZED RATS

Shipped to all points via Air Express
For further information write

HORMONE ASSAY LABORATORIES, Inc. • 808 E. 58th St.
Chicago 37, Ill.

WHITE RATS 40c and up

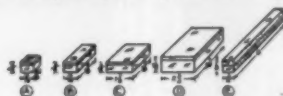
Rabbits, Cavies, White Mice, Ducks, Pigeons, Hamsters
Write • J. E. STOCKER • Ramsey, N. J.

The Market Place

SUPPLIES AND EQUIPMENT

TRANSPARENT BOXES

For Every Laboratory, Every Collector
of Small Objects, Every Home Workshop!



Five Sizes Now Available

Write for New Leaflet TR-S

R. P. CARGILLE
118 Liberty Street, New York 6, N. Y.

GLYCOCYAMINE—Hydroxyproline, L-Methionine
• AMINO ACIDS • BIOCHEMICALS
• PRE-MIXED MICROBIOLOGICAL ASSAY MEDIA
H. M. CHEMICAL COMPANY, LTD.
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RHEINBERGS RETICULES

Established
1884

MADE IN ENGLAND

BRITISH CRAFTSMANSHIP combines precision accuracy
and clarity with lowest prices

Complete list of

STOCK EYEPIECE & STAGE MICROMETERS from
RHEINBERGS LTD., 57/60 Nether Viaduct, London E.C.1, England
Cables: Rheinberg, London

PARASITOLOGICAL PREPARATIONS

• high quality — low priced. Write for catalog
TROPICAL BIOLOGICALS • P.O. Box 2227, San Juan, Puerto Rico.



QUARTZWARE

for laboratory and industry

A complete line of standard laboratory ware.
Also custom fabricating to meet your requirements.

For particulars, write: Quartzware Division

THE PANRAY CORP.

340 Canal Street, New York 13, N. Y.

STAINS

STARKMAN Biological Laboratory

• RARE
• COMMON
Price list on Request
• 461 Bloor St., W.
Toronto, Canada

All Amino Acids (natural, synthetic, unnatural),
Rare Sugars, Biochemical Products, Reagents, New Pharma-
ceuticals in stock. Write or phone PLaza 7-8171 for complete
price list.

BIOS LABORATORIES, INC. 17 West 60th Street,
New York 23, N. Y.

**there
must be
a reason**



Here are eight distinct reasons why **Haemo-Sol** is the preferred cleaner for laboratory glassware

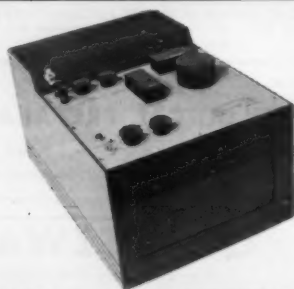
- Completely Soluble
- Leaves No Residue
- Fully Haemo-Digestive
- Lower Surface Tension
- Scientifically Formulated
- Controlled pH
- Multiple Laboratory Uses
- Greater Economy

for literature and samples
write

MEINECKE & COMPANY, INC.

225 Varick St.

New York 14, N. Y.



**FARRAND PHOTOELECTRIC
FLUOROMETER**

"One of the chief advantages of your fluorometer is its tremendous range of sensitivity"

The Farrand Fluorometer provides stability and linear response over a wide range of sensitivities for measurements of extremely low concentrations in Micro or Macro volumes of solution.

Suitable for all Fluorometric methods of analyses-Thiamin-Riboflavin-Vitamins and their derivatives-Quinine-Atabrine-Porphyrin-Chlorophyll-Drugs-Oils-Metal complexes, Organic or Inorganic compounds.

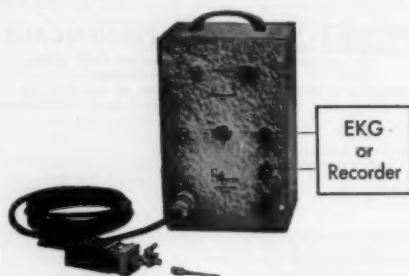
Bulletin 803 on request

FARRAND OPTICAL CO., Inc.

Precision Optics, Electronic and Scientific Instruments

BRONX BLVD. & E. 238TH ST. NEW YORK 66, N. Y.

STATHAM
Physiological Pressure Transducers



The Model P23 pressure transducers were specifically designed for the purpose of measuring and recording arterial and venous blood pressures. The system illustrated above demonstrates how simply measurements can be obtained with Statham transducers.

STATHAM
SL
LABORATORIES

SCIENTIFIC INSTRUMENTS

9328 Santa Monica Blvd., Beverly Hills, Calif.

Please write our
Engineering Department
for more specific data.



RESEARCH BIOCHEMICALS
for
**Biological & Microbiological
INVESTIGATIONS**



Uniform

Pre-tested

Dependable

"VITAMIN FREE" CASEIN

Hot Alcoholic Extracted

Exceptional in Purity for Vitamin Tests
TYPICAL VITAMIN ANALYSIS

(micrograms per gram)

THIAMINE	0.20
RIBOFLAVIN	0.60
NIACIN	0.25
PYRIDOXINE	0.70
PANTOTHENIC ACID	0.15
BIOTIN	0.0015
FOLIC ACID	0.030

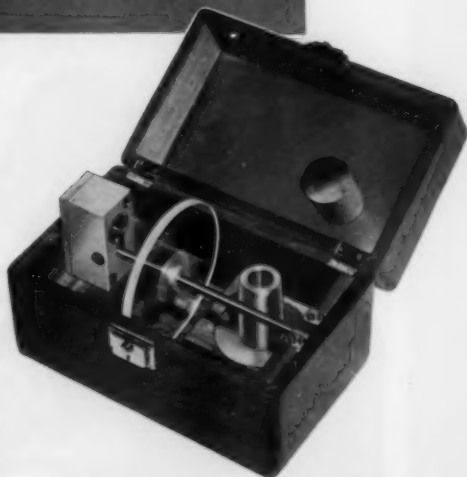
Now Available at New Reduced Prices
Write for Revised Catalogue S#850 Listing
a Complete Selection of Over 400
Important Biochemicals

NUTRITIONAL BIOCHEMICALS CORP.
CLEVELAND 5, OHIO



For Beta ray therapy of certain eye and skin conditions, Tracerlab has developed a Strontium Medical Applicator. This instrument is available for use by qualified physicians who are approved by the U. S. Atomic Energy Commission for this type of work.

The applicator consists of a source containing approximately 25 millicuries of Strontium-90 in equilibrium with Yttrium-90 mounted at the end of a 7 inch shaft. The source has an active diameter of 7.8 millimeters and is hermetically sealed. A $\frac{1}{4}$ inch sliding plexiglass shield is mounted on the shaft for the protection of the operator. When the instrument is fastened in its storage box the source is completely shielded by means of a source shield. A second shield is also provided for setting the applicator down on a table.



For further information on the Strontium Medical Applicator, write for Bulletin R-28.

Tracerlab →

TRACERLAB INC., 130 HIGH STREET, BOSTON 10, MASS.

Western Division
2295 San Pablo Ave., Berkeley 2, California
New York Office
General Motors Bldg., 1775 B'way, N. Y. 19
Midwest Office
LaSalle-Wacker Bldg., 221 N. LaSalle, Chicago

"Tailored" FOR TEACHING

— and **LOWEST** in Cost

Spencer Junior Stereoscopic Microscopes possess a unique combination of features valuable in classroom instruments. They are low in height and have slightly inclined eyepieces—as a result fatigue is reduced and students see clearly with comfort without straining necks and backs. Models with double revolving nosepieces require only a quick $\frac{1}{4}$ turn to switch from one power to another. Shielded by a circular housing, the paired objectives are completely protected from dust as well as abusive handling. Spencer Junior Stereoscopic Microscopes provide clear, erect images and wide, flat fields. Magnifications range from 6.8X to 98X. Priced well below other stereoscopic microscopes, they appeal to the school with a limited budget.



See your AO Spencer distributor for a demonstration or write Dept. H4.

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COMPANY
Instrument Division
Buffalo 15, New York

Makers of Microscopes for over 100 Years



